ABSTRACTS OF WORLD MEDICINE

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Pathology

EXPERIMENTAL PATHOLOGY

282. **The Significance of Shock in the Pathogenesis of Experimental Sepsis.** (Значение шока в патогенезе экспериментального сепсиса)
I. S. MASTBAUM. *Бюллетень экспериментальной Биологии и Медицины* [*Bjull. eksper. Biol. Med.*] **41**, 36–38, Feb., 1956. 2 refs.

In a study of the significance of shock in the pathogenesis of sepsis the author found it extremely difficult to induce traumatic shock in rabbits, but on the other hand the induction of shock by means of insulin was quite easy. In animals shocked by this method the course of an artificially produced streptococcal sepsis was much more severe than in the control animals. Even when the shock had been successfully overcome it was observed that a greater susceptibility to infection persisted in the shocked animals. *A. Orley*

283. **A and B Blood-group Antigens on Human Epidermal Cells Demonstrated by Mixed Agglutination**
R. R. A. COOMBS, D. BEDFORD, and L. M. ROUILLARD. *Lancet* [*Lancet*] **1**, 461–463, April 21, 1956. 3 figs., 5 refs.

Experiments were carried out at the University of Cambridge on suspensions of epithelial cells isolated from thin split-skin fragments obtained for plastic surgery and stored. It was demonstrated that the cells contained the same ABO antigens as did the donor's erythrocytes, and would combine specifically with anti-A or anti-B. This was shown by the fact that when erythrocytes of known ABO group were added to suspensions of epithelial cells, mixed agglutination occurred only with cells from donors of the same ABO group which had been treated with the corresponding antiserum.

The technique described is delicate, requiring siliconed glassware and careful controlling. *I. Dunsford*

284. **Plasma Protein Changes and their Influence on the Erythrocyte Sedimentation Rate in Myocardial Infarction.** [In English]
E. LINKO, E. WARIS, and H. A. ALIKOSKI. *Acta medica Scandinavica* [*Acta med. scand.*] **153**, 389–398, Jan. 31, 1956. 1 fig., 19 refs.

In a series of 49 proven and 8 doubtful cases of myocardial infarction at the Medical Clinic, University of Turku, Finland, the relation between the plasma protein level and the erythrocyte sedimentation rate (E.S.R.) was evaluated statistically.

The total plasma protein value, estimated by the Kjeldahl method and by either the Van Slyke falling-drop or the Antweiler electrophoretic micromethod, varied very little during the course of the disease. There was considerable variation, however, in the values for protein fractions as determined by Antweiler's method, a marked increase being observed in α_2 globulin and fibrinogen, with a corresponding decrease in the albumin and α_1-globulin fractions, reaching a peak at the end of the first week. The E.S.R., estimated by the Westergren technique, varied according to the extent of these changes, being highest when they were most pronounced. The β- and γ-globulin levels showed no correlation with the E.S.R., there being no significant fluctuations in these fractions during the early weeks of the illness.
M. Sandler

CHEMICAL PATHOLOGY

285. **Further Observations on the Diphenylamine (DPA) Reaction as an Index of Inflammation**
A. F. COBURN, R. C. BATES, J. W. HAHN, and P. MURPHY. *Journal of Chronic Diseases* [*J. chron. Dis.*] **3**, 140–153, Feb., 1956. 5 figs., 15 refs.

A further evaluation of the diphenylamine (DPA) reaction was made at Northwestern University Medical School, Chicago, in the course of a search for the most accurate and sensitive laboratory methods for the assessment of activity in rheumatic fever, particularly of low-grade activity, which is of importance in ensuring that steroid therapy has been adequate, and also in cases in which cardiac surgery is contemplated.

Investigations into the cause of the reaction (the results of which are to be published in detail elsewhere) showed that the colours produced by the addition to serum of the acid blank reagent (without DPA) and of the DPA reagent are both measures of the presence of the same material (probably degradation products of muco-proteins) and differ only in their intensity. The subtraction of the spectrophotometric reading for the acid blank reagent from that for the DPA reagent to produce a " corrected " result, as formerly practised, is thus unjustified and lessens the sensitivity of the test.

The DPA reaction was determined and the C-reactive protein test carried out on 761 specimens of serum from 107 cases of rheumatic fever among U.S. Navy recruits and 6 in children. The results of these tests were compared and related to the clinical state of activity. In

general the clinical signs subsided first, followed later by the return to normal of the C-reactive protein reaction and finally by that of the DPA reaction. A rise in the DPA value often preceded a relapse or exacerbation, the C-reactive protein reaction usually becoming positive simultaneously or slightly later.

It is concluded that the DPA test, although non-specific for rheumatic fever, appears to be the most sensitive and helpful method available for the assessment of activity in the management of rheumatic fever.

Harry Coke

286. **Glucagon-induced Hyperglycemia as an Index of Liver Function**

T. B. VAN ITALLIE and W. B. A. BENTLEY. *Journal of Clinical Investigation* [*J. clin. Invest.*] **34**, 1730–1737, Dec., 1955. 3 figs., 25 refs.

Glucagon is a protein which can be extracted from the pancreas, and which on intravenous administration induces a rise in the blood sugar level. It increases the concentration of phosphorylase in liver slices *in vitro*, and it is accepted that its action *in vivo* is due to an increase of liver glycogenolysis. Glucagon does not accelerate the breakdown of glycogen in muscle, but seems rather to stimulate glucose uptake by the peripheral tissues.

Since the diseased liver usually has a reduced glycogen content the degree of hyperglycaemia induced by glucagon might be a useful index of liver function. Working at St. Luke's Hospital, New York, the authors have investigated this possibility in experiments on 10 healthy subjects and 8 patients with severe parenchymatous liver disease. In addition to glucagon, a small amount of adrenaline was given to prevent increased utilization by the peripheral tissues of the sugar released from the liver. The procedure adopted was first to give 0·003 mg. of adrenaline per kg. body weight subcutaneously, and 10 minutes later 0·03 mg. of glucagon per kg. intravenously in 150 ml. of saline, the duration of the infusion being approximately 30 minutes. The blood sugar level was determined at the start of the experiment and again at the end of the infusion of glucagon and 25, 50, and 75 minutes later. The blood sugar level in the normal subjects rose to a maximum of 65 to 100 mg. per 100 ml. above fasting level, whereas in the patients with liver disease the maximum rise averaged 25 mg. per 100 ml., and was never so high as 50 mg. per 100 ml. The authors therefore conclude that this procedure "has potential value as an index of one aspect of liver function".

H. Lehmann

287. **Plasma Fibrinolytic Activity in Cirrhosis of the Liver**

H. C. KWAAN, A. J. S. MCFADZEAN, and J. COOK. *Lancet* [*Lancet*] **1**, 132–136, Jan. 21, 1956. 3 figs., 14 refs.

A study of the fibrinolytic activity in the plasma of 30 cases of cirrhosis of the liver by the quantitative technique described by Biggs and MacFarlane is reported. Fibrinolysis was complete in less than 6 hours in 7 cases, between 6 and 12 hours in 9, and between 12 and 24 hours in 5. In the remaining 9 cases there was a loss of 25 to 67% of the initial levels. The average reduction in fibrin content after incubation for 24 hours was 83%. These findings are contrasted with those obtained in 12 cases of primary carcinoma arising in cirrhotic livers and in 20 healthy controls. In the former the average reduction in fibrin after incubation for 24 hours was 12%, and in the latter 13%. No relationship was observed between the severity of the cirrhosis and intensity of the fibrinolysis.

Splenectomy in 6 patients with cirrhosis caused immediate intensification of the fibrinolytic activity—an influence which passed off within 4 hours. It is in this period that there is risk of haemorrhage associated with fibrinolysis. Within 24 hours of operation spontaneous fibrinolytic activity ceased. The subcutaneous injection of adrenaline in 6 cases of cirrhosis led to increased fibrinolytic activity, which was on the average of greater intensity and of longer duration than that in healthy controls. Corticotrophin administered to 2 of the cases showing active fibrinolysis led to a significant reduction in the fibrinolytic activity on the fifth day. It is concluded that suprarenal cortical activity depresses the spontaneous fibrinolytic activity of the plasma, and may play a part in the development of thrombosis of the portal vein observed postoperatively or during corticotrophin therapy in cirrhosis of the liver. The findings in 1 case of cirrhosis of the liver in which portal-vein thrombosis developed during the administration of corticotrophin are reported. At the time when the thrombosis developed, fibrinolytic activity was absent but a month later it was intense.

The fibrinolysin had no influence on fibrinogen, and it is concluded that it is not plasmin but is similar to cadaveric fibrinolysin described by Mole (*J. Path. Bact.*, 1948, **60**, 413).—[Authors' summary.]

288. **A Quantitative Chemical Test for "Microscopic Haematuria"**

H. W. BALME, A. E. DORMER, and L. RAWLINGS. *British Medical Journal* [*Brit. med. J.*] **1**, 612–614, March 17, 1956. 1 fig., 8 refs..

The authors, working at St. Bartholomew's Hospital, London, have applied the amidopyrine test to the quantitative estimation of blood in the urine. The use of a chemical method instead of the usual microscopical examination of the centrifuged deposit and enumeration of the erythrocytes seen in an average field eliminates errors arising in the latter from variations in the rate of centrifugation and in sampling, and from the presence of crystals which may be difficult to distinguish from erythrocytes under the low power of the microscope. The technique is as follows. Two samples of the urine, 5 ml. and 10 ml. in volume respectively, are placed in separate conical tubes and centrifuged for 10 minutes at 3,000 r.p.m. All but 0·2 ml. of the supernatant fluid is removed and the volume made up to 1 ml. with distilled water. Then 0·2 ml. of 30% acetic acid is added, followed by 1 ml. of alcoholic amidopyrine and 3 drops of 20-volume hydrogen peroxide. The tubes are then shaken well and left to stand for 3 minutes.

A positive reaction is indicated by the development of a lilac or mauve colour. If neither tube shows this change the urine is reported as containing fewer than 5,000 erythrocytes per ml. If the 10-ml. sample gives a positive and the 5-ml. sample a negative reaction, approximately 5,000 erythrocytes per ml. are present. If both are positive, serial dilutions of urine with normal urine or saline are made and the test repeated with 5 ml. of each dilution. The highest dilution that just gives a positive reaction is noted, and multiplication of the dilution factor by 10,000 gives the number of erythrocytes present in 1 ml. of the urine.

The authors point out that difficulties may arise with highly pigmented urines, and that a false positive reaction may occur if the urine contains iodides. They also point out that although, for convenience, the result is given in terms of the erythrocyte content, the development of the colour is actually related to the haemoglobin content, and allowance must be made for this if the mean corpuscular haemoglobin content is markedly abnormal. It is not suggested that this method should supersede microscopy of the centrifuged deposit, which is still necessary to determine the presence or absence of formed elements other than erythrocytes. However, it has been found to be of value, particularly in the management of cases of acute nephritis and subacute bacterial endocarditis and in the control of anticoagulant therapy.

Victor M. Rosenoer

MORBID ANATOMY AND CYTOLOGY

289. **Sclerosing Hemangioma (Histiocytoma, Xanthoma) of the Lung**

A. A. Liebow and D. S. Hubbell. *Cancer* [*Cancer* (*N.Y.*)] **9**, 53–75, Jan.–Feb., 1956. 40 figs., 22 refs.

The authors record, from Yale University School of Medicine, 7 cases of sclerosing haemangioma of the lung, 5 in women between the ages of 15 and 50, of which 4 were discovered accidentally on routine radiography. The tumours were characterized by the proliferation of blood vessels of varying calibre. They were usually spherical in shape, ranging in size from 1·5 to 8 cm. in diameter, were surrounded by a fibrous capsule, were unconnected with the bronchial tree, and were largely composed of haemangiomatous, partly cavernous, formations supported by mesenchymal cells of fibroblast or reticulum-cell type. Areas of hyaline fibrosis alternated with areas where haemorrhage had occurred, as evidenced by siderosis and cholesterol-crystal clefts, and were interspersed with larger spaces filled with free neutral fat. Portions of lung parenchyma had become trapped within these masses, displaying papillary infoldings, the alveolar cells frequently assuming cuboidal shape. It is noteworthy that all the tumours were in the lower lobe, generally the right. Lobectomy appeared to be curative. A useful case summary is appended.

[These tumours may well be hamartomatous in origin and are reminiscent of tumours of similar composition found in the mediastinum and retroperitoneum.]

R. Salm

290. **The Anatomical Approach to the Study of Smoking and Bronchogenic Carcinoma. A Preliminary Report of Forty-one Cases**

O. Auerbach, T. G. Petrick, A. P. Stout, A. L. Statsinger, G. E. Muehsam, J. B. Forman, and J. B. Gere. *Cancer* [*Cancer* (*N.Y.*)] **9**, 76–83, Jan.–Feb., 1956. 8 figs., 2 refs.

At the Veterans Administration Hospital, East Orange, New Jersey, the authors have examined serial sections of the bronchial tree of 41 male patients, of whom 14 (all moderate to heavy smokers) died of bronchial carcinoma and 27 (8 non-smokers, 14 light or moderate smokers, and 5 heavy smokers) died of extrapulmonary cancer, the results in these two groups being then compared in various ways.

The changes observed in the bronchial mucosa were those of basal-cell hyperplasia, stratification, and squamous metaplasia, and they were correlated in degree with the smoking habits of the subjects. The preliminary data obtained, which did not take into account the age [nor, apparently, the length of exposure to tobacco smoke], showed that basal-cell hyperplasia was present to a greater degree in smokers than in non-smokers, whereas the difference of stratification and squamous metaplasia between these two groups was less pronounced. The authors are well aware that the series was small and highly selected.

R. Salm

291. **The Pathology and Bacteriology of Resected Lesions in Pulmonary Tuberculosis**

H. C. Sweany and H. H. Seiler. *Diseases of the Chest* [*Dis. Chest*] **29**, 119–152, Feb., 1956. 36 figs., 22 refs.

In this paper from the Southwest Florida Tuberculosis Hospital, Tampa, Florida, the authors discuss the pathological and bacteriological findings in resected pulmonary tissue from 34 patients who had received chemotherapy for tuberculosis.

In 9 cases there was complete closure of cavities; it is considered likely that recovery would have taken place in these cases without surgical treatment, since a positive culture was obtained from resected tissue in only one instance. In 2 cases the radiograph did not show cavitation, but operation was justified because resected material was positive on both culture and smear examination in one case and on culture only in the other. There were 3 fatal cases in the series. The remaining 20 cases showed residual cavities after chemotherapy, acute pneumonic spread, large caseous masses, or (the largest group) a mixture of these. In 3 cases the smears from the specimens were positive and the cultures negative—perhaps because the bacilli, though alive, were no longer harmful. The authors state that the "specimen and even the sputum does not need to be negative to obtain a good surgical result".

It is concluded from the findings that in about 25% of all cases healing is achieved by chemotherapy without surgery, in 60% operation is necessary for recovery, while in 15% surgical removal of diseased tissue, although not essential for survival, has such a good moral effect on both clinician and patient that it is held to be justified.

J. B. Wilson

292. **The Pulmonary Vessels in Patent Ductus Arteriosus**
D. HEATH and W. WHITAKER. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **70**, 285–290, 1955. 7 figs., 5 refs.

The pulmonary vessels were examined histologically in biopsy specimens obtained at thoracotomy from 9 cases of patent ductus arteriosus and in necropsy specimens from 3 further cases at the City General and Royal Hospitals, Sheffield. In 2 cases in which a moderate degree of pulmonary hypertension had been demonstrated by cardiac catheterization medial thickening of the pulmonary arteries was present, and in 2 cases in which the pulmonary arterial pressure was greatly increased medial necrosis and occlusion of the lumen of muscular vessels by fibrous tissue were also seen. The pulmonary vessels were unchanged in the remaining cases, in which the pulmonary arterial pressure was normal. *J. B. Enticknap*

293. **The Electron-microscopy of Atheroma**
C. I. LEVENE. *Lancet* [*Lancet*] **2**, 1216–1217, Dec. 10, 1955. 8 figs., 10 refs.

It has been maintained for some nine years by Duguid (*J. Path. Bact.*, 1946, **58**, 207; *Abstracts of World Medicine*, 1947, **1**, 393) that the atherosclerotic plaque, as seen in man, is to a great extent the product of organized thrombosis in the vessel walls. According to this thesis, although the fibrous tissue which forms the plaque gives all the staining reactions ascribed to collagen, it consists in reality of fibrin, and represents mural thrombi covered by endothelium and thus incorporated into the wall of the vessels. In order to test Duguid's theory, typical atherosclerotic plaques were examined by the author by means of electron microscopy at the Royal Victoria Infirmary, Newcastle upon Tyne.

The examination of standard examples of normal collagen obtained from human tendo Achillis and elsewhere showed its characteristic electron-microscopic features to be a transverse periodicity of about 640 Å. (1 μ=10,000 Å.) and a fibre width of 350 to 800 Å. Standard examples of fibrin, prepared by adding calcium chloride to human plasma, showed a regular periodicity of about 230 Å. Four grids were prepared from each specimen and 4 to 8 representative fields were photographed at a magnification of $\times$11,300 and enlarged photographically to one of $\times$67,800.

Atheromatous plaques taken at random from 15 human aortas were then examined. All gave the staining reactions ascribed to collagen, but in addition 7 of the 15 plaques showed fibrinous material lying either superficially or in the deeper layers of the thickened intima. All intimal plaques, even those devoid of stainable fibrin, gave a periodicity of 230 Å. The same fibres of 230-Å. periodicity, when treated with chymo-trypsin for 2 hours, were partially digested—collagen remains virtually unaffected by trypsin—suggesting that these fibres consisted of fibrin. Finally, 5 samples of intima from apparently normal aortas (the youngest subject being aged one year and the oldest 65 years) were examined. In none of the specimens was collagen found, and the fibres in all cases were identical on ultramicroscopical examination with those in the atheromatous plaques, that is, with a periodicity of 230 Å.

The author suggests that these experiments show that the different forms of connective tissue cannot be identified solely by their staining reactions. They further support the hypothesis that mural thrombosis by the deposition of fibrin from the bloodstream and by its incorporation into the intima may produce a fibrous thickening which is indistinguishable from atherosclerosis. *Z. A. Leitner*

294. **The Pathological Anatomy of Idiopathic Myocarditis.** (К патологической анатомии идиопатического миокардита)
B. S. SVADKOVSKII. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **34**, 67–71, No. 2, Feb., 1956. 3 figs., 12 refs.

The author describes the pathological findings in a young woman of 22 who died suddenly at work, having complained for about a year of dyspnoea, pains in the region of the heart, and exhaustion. At necropsy the heart was found to weigh 600 g. The left ventricle was enlarged and dilated, its walls being 2 cm. thick, the valves were transparent, the chordae tendineae thin, and the papillary muscles hypertrophied; the right ventricle was slightly hypertrophied and its walls 0·4 cm. thick. On the intima of the aorta and coronary arteries there were isolated patches of atherosclerosis. On section the heart muscle was compact and lustreless, and contained whitish streaks which in the interventricular septum formed cicatricial areas 2·5 $\times$ 3 cm. in average dimensions. The histological appearances were those of "isolated" idiopathic myocarditis, with infiltration by histiocytes, lymphoid elements, and neutrophil and a few eosinophil granulocytes. There was necrobiosis of some of the muscle fibres with fragmentation of their nuclei. More widely met with were areas of well-marked dystrophic change in the myocardium, the fibres of which showed indistinct outlines, disappearance of the transverse striations, commencing liquefaction, and degeneration of the nuclei. Rapoport in his description of the disease describes these two types of change as inflammatory-infiltrative and dystrophic respectively. In this case not only were both types present, but also in wide areas the gradual replacement of the dystrophic muscle fibres by argyrophil fibres and finally by fibrous tissue and the disorganization of the elastic tissue of the smaller vessels characteristic of the later stages.

The aetiology of the disease is obscure; cases have been reported as following trauma, food poisoning, infections such as carbuncles, burns, rheumatism, trichinosis, uraemia, vaccination, pregnancy, and prolonged treatment with caffeine, arsphenamine, and sulphonamides. In some cases viruses and staphylococci have been isolated, but in the majority no bacterial cause has been found and an infective origin of the disease cannot be proved. Rapoport holds that all varieties of idiopathic myocarditis are attributable to the same allergic type of hyperreactivity of the organism, in which reflex nervous influences play an important part. Thrombosis of small blood-vessels is an integral part of the

pathological process and not a mere incident, and it is justifiable to call the disease " thrombomyocarditis ".

Clinically, two forms of the disease have been distinguished by Saphir—the acute, swiftly leading to acute heart failure and death; and the subacute, lasting some months, from which recovery is possible, though sudden death commonly occurs. Embolism, leading to hemiplegia and other complications, is not infrequent. The presenting symptoms are pains in the cardiac area, cyanosis, dyspnoea, tachycardia, and various forms of arrhythmia, including auricular fibrillation, extrasystoles, and A-V block. The temperature may be subfebrile and the erythrocyte sedimentation rate, although increased at first, may later return to normal. There is a moderate leucocytosis. The electrocardiogram indicates widespread and severe myocardial damage. At times severe attacks of pain simulating acute cholecystitis or some other abdominal condition may occur.

L. Firman-Edwards

295. **Vascular Obstruction in Chronic Pyelonephritic Kidneys and its Relation to Hypertension**
P. KINCAID-SMITH. *Lancet* [*Lancet*] **2**, 1263–1269, Dec. 17, 1955. 12 figs., 31 refs.

Obstructive vascular lesions and associated ischaemic renal parenchymal lesions in hypertensive chronic pyelonephritis are described. The renal parenchymal lesions in 45 consecutive necropsy cases of chronic pyelonephritis are compared, and differences between the hypertensive and normotensive cases are described. Because the nature of the vascular lesions in cases of chronic pyelonephritis suggested that they were the result of inflammation, 50 necropsy kidneys showing acute pyelonephritis were studied. Destructive lesions of the arterial walls and obstructive lesions of the lumen were found in these cases.

These findings are discussed in relation to their importance both in the pathogenesis of contracted pyelonephritic kidneys and in the development of hypertension in pyelonephritis. Ischaemic parenchymal lesions such as are described here in chronic pyelonephritis are also found in other conditions in which renal vascular obstruction is known to be associated with hypertension. In view of this the ischaemic lesions are thought to be causally related to the development of hypertension in chronic pyelonephritis.—[Author's summary.]

296. **The Relation of Portal Cirrhosis to Hemochromatosis and to Diabetes Mellitus**
E. T. BELL. *Diabetes* [*Diabetes*] **4**, 435–446, Nov.–Dec., 1955. 2 figs., bibliography.

The author has reviewed the findings in 932 cases of clinical portal cirrhosis coming to necropsy at the University of Minnesota between 1911 and 1953, cases of obstructive biliary cirrhosis and acute necrosis of the liver being excluded. The incidence of cirrhosis among all subjects over the age of 40 was 1·7%; there was only a small preponderance of males (1·75% compared with 1·62% in females) when allowance was made for the greater number of males examined (633 to 299).

Grouping according to the degree of haemosiderosis showed: (1) 11 cases of typical " bronze diabetes " with the complete syndrome of cirrhosis, haemosiderosis, diabetes, and melanoderma; (2) 18 cases in which all these features were present except for the skin pigmentation; (3) 8 cases of severe cirrhosis with varying degrees of haemosiderosis of the liver (one with melanoderma), but no clinical diabetes although hyaline islets were found in the pancreas; (4) 186 cases of pigmentary cirrhosis in which no clinical evidence of diabetes was found; in 28 of these cases microscopical examination showed abundant iron in every lobule (Grade 3), and often also in the portal tissues; six of these subjects had melanoderma, and marked haemosiderosis was also found in 14 of the 28 cases in which the pancreas was examined, although none of these patients had had glycosuria. It seems that pigmentary cirrhosis appears as frequently in females as in males, but does not progress to a severe degree so often.

The study showed that diabetes is about five times as frequent in cirrhotic males as in the general male (necropsy) population, but is not significantly increased among cirrhotic females. In the present series the incidence was 11·8% in cirrhotic males over the age of 40, compared with 2·32% in all males of the same age examined post mortem, while the corresponding figures for women were 6·7 and 4·98%. The incidence of diabetes (40%) was increased in cases of severe haemosiderosis, but not very greatly in those with lesser degrees of hepatic iron deposition. The study also revealed 40 cases of primary carcinoma of the liver (35 in 633 men and 5 in 299 women), the incidence thus being three times greater in males.

The author concludes that haemochromatosis is not a sharply defined entity but rather blends gradually with ordinary portal cirrhosis. The relationship between diabetes and haemochromatosis is obscure, but the high incidence of diabetes among men with non-pigmentary cirrhosis suggests that factors other than haemosiderosis are important.

[This paper contains much useful information and should be read in full.] *T. D. Kellock*

297. **Hepatic Regeneration. I. Course and Consequences in Acute Diffuse Parenchymatous Hepatitis.** (La régénération hépatique. I. Ses modalités et ses conséquences dans l'hépatite parenchymateuse diffuse aiguë)
G. ALBOT and C. NÉZELOF. *Presse médicale* [*Presse méd.*] **63**, 1813–1817, Dec. 25, 1955. 13 figs.

That the liver possesses a considerable capacity for regeneration has been demonstrated experimentally, and the extent of recovery after hepatic damage depends on this power. The normal and abnormal reparative mechanisms which determine the structural changes of cirrhosis after severe and prolonged hepatitis, however, are better known than those which follow acute and benign forms, although they can be studied histologically by puncture biopsy. The changes in acute diffuse parenchymatous hepatitis are described in this paper from the Hôtel-Dieu, Paris, with reference to 5 cases, of which 3 were cases of epidemic viral hepatitis, one was associated with cholelithiasis, and one was of indefinite aetiology—possibly viral, possibly toxic.

In the liver the process of regeneration reproduces the normal organogenesis of the hepatic lobule, being concerned under normal circumstances solely with the maintenance of its structure. This function is subserved by certain cells, smaller and more basophilic than the ordinary liver cell and situated at the periphery of the lobule. During the early stages of diffuse parenchymatous hepatitis proliferation of these dark cells may be observed in addition to the parenchymal lesions, which consist fundamentally in a " clarification " of the hepatic cells, associated with a disturbance of water and sugar metabolism and due to distension and oedema of the cells, particularly in the central part of the lobule. This is followed by homogeneous degeneration or acidophilic necrosis, usually confined to cells in the centre of the lobule, and a mesenchymatous inflammatory reaction consisting in oedema and distension of the Kupffer cells and infiltration of the portal spaces by mononuclear cells.

Regeneration is characterized by great activity of young hepatic cells, which are unequal and small in size, their cytoplasm being basophilic, dense, and rich in ribonuclein (electively staining with pyronin). [A few excellent photomicrographs illustrate these changes.] The density of the cytoplasm is due mainly to the presence of mitochondria, the cells being intensely siderophilic and staining black with iron haemotoxylin. The regenerative cells contain a considerable amount of glycogen and their nuclei are voluminous; they are often confused with atrophic degenerative cells, which are easily recognizable, however, by their eosinophilic plasma, their centrilobular localization, their pyknotic nuclei, and their complete lack of ribonuclein. A new generation of liver cells takes the place of the destroyed or altered cells, usually within a month. However, if there are extensive and massive lesions, leaving persistent areas of degeneration, the regenerated tissue appears to be oedematous, occupying all the periphery of the lobule. If regenerative activity is exceptional it may temporarily distort the structure of the liver lobule and also disturb biliary evacuation. *E. Forrai*

298. **Effects of Alcohol on Gastric Mucosa**
A. WYNN WILLIAMS. *British Medical Journal* [*Brit. med. J.*] **1**, 256–259, Feb. 4, 1956. 24 refs.

The author, at the University of Edinburgh, has examined specimens of gastric mucosa obtained from 25 adults with a history of alcoholism, 16 specimens being obtained at biopsy, 6 at necropsy, and 3 at operation for peptic ulcer. The mucosa was normal in 9 cases, in some of which there had been marked alcoholism for several years with delirium tremens, and necropsy revealed fatty changes in the liver. Mild to moderate inflammation was found in 7 cases and chronic atrophic gastritis in 6.

In animal experiments varying volumes and concentrations of ethyl alcohol were introduced into the stomachs of guinea-pigs. Concentrations of 20% or greater resulted in hyperaemia, desquamation, and necrotic foci, leading to erosions, haemorrhage, and ulcers. The higher the concentration and the greater the volume of alcohol, the more severe were the lesions; furthermore the lesions tended to be more severe when alcohol was given in the fasting state than when it was given after food. Since gin and whisky have an alcohol concentration of about 40% and port and sherry one of 20% it is considered " reasonable to assume " that the consumption of large amounts of these " may lead to haemorrhages, erosions, or ulcers in human beings ".

This investigation shows that long-continued alcoholism may have no lasting effect on the stomach and that only in a minority of cases does it produce more than mild chronic gastritis. [This finding is in agreement with those of previous investigations, including the excellent one by Palmer (*Medicine* (*Baltimore*), 1954, **33**, 199).] However, the author suggests that the repeated erosions in chronic alcoholism may be the cause of some cases of atrophic gastritis. The healing of experimentally induced gastric ulcers in guinea-pigs was sometimes delayed by the instillation of alcohol, and the author therefore considers that there is some justification for advising patients with peptic ulcer to avoid strong alcoholic drinks. *M. C. Berenbaum*

299. **Exfoliative Cytology in Chronic Ulcerative Colitis**
J. T. GALAMBOS, B. W. MASSEY, M. I. KLAYMAN, and J. B. KIRSNER. *Cancer* [*Cancer* (*N.Y.*)] **9**, 152–159, Jan.–Feb., 1956. 9 figs., 7 refs.

The authors have studied, at the University of Chicago, the exfoliative cytology of the colon in 31 patients with proven chronic ulcerative colitis, and compared it with that in a control group of 17 patients suffering from other intestinal, non-malignant conditions; the cells were obtained by colonic washing or by an irrigation-suction method. They state that while they were able to differentiate the atypical epithelial cells obtained from cases of ulcerative colitis in remission from those obtained from cases with superimposed malignancy, the usefulness of the method was severely limited by the demonstration that during the acute phase of the illness the cells obtained were indistinguishable from malignant cells, but suggest that further studies along these lines are " clearly indicated ". *R. Salm*

300. **Verrucous Naevi**
H. HABER. *Transactions of the St. John's Hospital Dermatological Society* [*Trans. St John's Hosp. derm. Soc.* (*Lond.*)] No. 34, 20–28, 1955. 13 figs., 6 refs.

The aetiology and clinical characteristics of many forms of verrucous naevi are described and the differential diagnosis is discussed. Since the clinical and the microscopical appearances of individual lesions vary considerably the present author selected, from 82 cases examined histologically at St. John's Hospital for Diseases of the Skin, London, 10 classic examples showing different histological pictures but basically exhibiting the same features. Each case is briefly described and illustrated by reproductions of photomicrographs. The author suggests that since some of the naevi may be malignant, treatment in all cases should be by total excision rather than electrosurgery; further, a thorough histological examination should be carried out in all cases. *G. B. Mitchell-Heggs*

Microbiology and Parasitology

301. **Possible Infection of Man by Indirect Transmission of *Trichophyton discoides***
J. WALKER. *British Medical Journal* [*Brit. med. J.*] 2, 1430–1431, Dec. 10, 1955. 7 refs.

In studies carried out at the London School of Hygiene and Tropical Medicine the author has attempted to prove, by means of various experiments, the theory of indirect transmission of *Trichophyton discoides*, which theory would explain the increasing number of cases of cattle ringworm seen in patients who have had no direct contact with either an infected animal or another infected person. Scrapings taken from the walls of cow stalls, cow sheds, scratching posts, and fence rails, and samples of cow dung and of soil taken from the base of scratching posts at three different farms were examined microscopically for the presence of hair and epithelial scales, and selected portions plated out for culture.

Nearly all the specimens taken from the woodwork and the soil gave positive results, and in three instances the trichophyton could be grown. In contrast to this, the samples from the cow dung yielded only negative results. In further experiments, the results of which also support the theory of indirect transmission, it was shown that out of 50 samples of *Trichophyton discoides* kept in folded paper at room temperature, 29 were still viable after 15 months. However, experiments undertaken in order to test the ability of the fungus to survive in a saprophytic form under natural conditions gave inconclusive results. The author states that the possibility that infection may occur by parasitic spores of the fungus, or by conidia formed by growing in soil and in animal droppings, can be only " tentatively concluded ".

A. Fessler

BACTERIA

302. **Atypical Anaerobic Forms of *Streptococcus pyogenes* Associated with Tetracycline Resistance**
E. J. L. LOWBURY and L. HURST. *Journal of Clinical Pathology* [*J. clin. Path.*] 9, 59–65, Feb., 1956. 2 figs., 13 refs.

The first-named author, with Cason (*Brit. med. J.*, 1954, 2, 914), has previously reported the occasional emergence of strains of *Streptococcus pyogenes* resistant to the tetracycline group of antibiotics during the treatment of burns with aureomycin by mouth, these organisms growing well both aerobically and anaerobically. The present authors now describe, from Birmingham Accident Hospital, streptococci isolated in similar circumstances which, however, grew anaerobically but not aerobically on ordinary media, though they grew aerobically when the concentration of agar was raised. These forms seem to be related to the development of tetracycline resistance, since erythromycin was always effective in eliminating the strains from the burn lesions. The interference by these organisms with the taking of skin grafts was similar to that of aerobic *Str. pyogenes*, and they were also associated with suppuration and other local signs of infection. In the course of serological studies three different agglutination patterns were found, though most conformed to the 5/27/44 pattern or a related one. Cultures of the strains on Dorset's egg medium or on blood–agar often grew aerobically after 48 hours at room temperature when subcultured on to nutrient broth or blood–agar. Tetracycline resistance did arise in one strain after several days' standing on Dorset's medium, although a resistant strain was produced by the patient on the same day. The authors point out that these forms are anaerobic only in certain media, so that " conditional aerobiosis " would be a more descriptive term for the phenomenon. They suggest the possibility that production of hydrogen peroxide may explain the preference of these strains for anaerobic conditions; for when they were grown aerobically on concentrated agar (with serum) or anaerobically on ordinary serum–agar hydrogen peroxide was not produced, whereas abundant hydrogen peroxide appeared during aerobic culture on ordinary serum–agar. There was no difference between the sensitivity of the aerobic streptococci and of these anaerobic strains to the bactericidal action of peroxide. The authors believe that these anaerobic forms arise independently and not from cross-infection from a single mutant, and that the reversion to aerobiosis seems to be the final stage in the production of tetracycline resistance.

J. G. Jamieson

303. **Studies of Bacterial Throat Flora during Chemoprophylaxis of Rheumatic Fever**
J. M. MILLER and B. F. MASSELL. *New England Journal of Medicine* [*New Engl. J. Med.*] 254, 149–154, Jan. 26, 1956. 1 fig., 35 refs.

The bacteriology of the throat of 119 patients with a history of acute rheumatic fever who were receiving prolonged treatment with sulphadiazine or penicillin was compared with that of 94 patients with a similar history who were not receiving chemoprophylaxis. The investigation, which was carried out at the House of the Good Samaritan, Boston, extended over 12 months, throat swabs being taken at intervals throughout this period. Of the treated patients, 59 received penicillin and 60 sulphadiazine.

The medium used, sheep-blood–agar, does not support the growth of *Haemophilus influenzae*; therefore no information concerning the presence or absence of this organism is available. The incidence of *Streptococcus viridans* and of *Staphylococcus albus*, the most commonly found organisms, was the same in both of the treated groups and the control group. The incidence of *Staph. aureus* was higher in the two treated groups than in the

controls, whereas pneumococci were more frequently present in the control group than in either of the treated groups. None of the throat swabs from the patients receiving penicillin or sulphadiazine yielded Group-A beta-haemolytic streptococci. Coliform bacilli were isolated from throat swabs from 10% of the penicillin-treated patients, but in none of these was there clinical superinfection of the respiratory tract by the organisms. No information was available concerning fungus infections, but there were no clinical manifestations of moniliasis in the series. *E. G. Rees*

304. **The Hospital Staphylococcus. A Comparison of Nasal and Faecal Carrier States**
J. BRODIE, M. R. KERR, and T. SOMMERVILLE. *Lancet* [*Lancet*] **1**, 19–20, Jan. 7, 1956. 3 refs.

In view of the increasing frequency with which staphylococcal disease is being acquired in hospitals the authors, working at King's Cross Infectious Diseases Hospital, Dundee, have determined the nasal and faecal staphylococcal carrier rate among 56 ward patients, 127 patients on the day of admission, and 74 of these patients after a week in hospital. This showed that on admission 20% of the patients were nasal carriers and 17% faecal carriers; one week later both these rates had risen to 38%, which was almost the same as those among the patients already in hospital at the start of the investigation. Staphylococci of serological type ac/- rose from 6 to 27% in the nose and from 6 to 35% in the faeces; the number of other serotypes fell. Sensitivity tests showed that these strains were generally resistant to most of the usual antibiotics, and that although the nasal strains remained sensitive to chloramphenicol, the faecal strains were resistant to this and all the other antibiotics tested. All strains isolated after one week in hospital, however, were still sensitive to erythromycin.

The authors suggest that the appearance of these staphylococci in the faeces may well account for the increase of enterocolitis in hospital patients, since it has been shown that the predominant enterotoxin-producing type of staphylococcus found post mortem in the intestine of patients treated with antibiotics is probably the same as serotype ac/-. The study seems to show that the faecal carrier is likely to be a more important source of hospital cross-infection than the nasal carrier. The authors suggest that serological typing of staphylococcus is more suitable for use in hospital laboratories than the more complicated phage-typing, and could be used for tracing sources of infection. *R. F. Jennison*

305. **Evaluation of the "Positive" Urine Culture. An Approach to the Differentiation of Significant Bacteria from Contaminants**
J. P. SANFORD, C. B. FAVOUR, F. H. MAO, and J. H. HARRISON. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 88–93, Jan., 1956. 16 refs.

To reduce the difficulty of determining whether the presence of bacteria in urine indicates a clinically significant infection of the urinary tract, the authors, working at the Peter Bent Brigham Hospital (Harvard Medical School), Boston, use a quantitative method in which agar pour plates are made from specimens of urine collected with aseptic precautions. With this method they have found that unless there are at least 1,000 viable organisms per ml. of urine active infection of the urinary tract is improbable, and that if the urinary concentration is less than this the organisms are probably contaminants.

Microscopical examination of smears made from the sediment after centrifugation of 8 to 10 ml. of urine showed that the presence of a moderate number of bacteria generally indicates infection, but that the presence of leucocytes is a less reliable guide.

R. Hare

SEROLOGY AND IMMUNOLOGY

306. **Antigenicity Studies on Salk-type Poliomyelitis Vaccine**
D. TYRRELL, S. A. KEEBLE, and W. WOOD. *British Medical Journal* [*Brit. med. J.*] **1**, 598–601, March 17, 1956. 3 figs., 6 refs.

In 1955 pilot quantities of poliomyelitis vaccine were prepared in the United Kingdom from the same three strains of virus that had been used in preparing the Salk poliomyelitis vaccine for the United States field trials in 1954. In this paper the authors report the serological responses to immunization with a batch of this vaccine in 15 volunteers (medical staff and students), and compare these with the results of potency tests carried out with the vaccine on mice and rhesus monkeys. The mice were given three injections intraperitoneally of 0·5 ml. each of the vaccine, either undiluted or diluted 1 in 5, at weekly intervals; the monkeys received three intramuscular injections each of 1 ml. of the vaccine, undiluted or diluted 1 in 10, the second dose being given one week after the first, and the third 4 weeks after the second. The human subjects received the same dose of undiluted vaccine by deep intramuscular injection at the same intervals as those used for the monkeys. No local reactions were observed.

In the mice the maximum serum antibody titre produced against any of the virus types was only 1 in 32, but 45% of the animals immunized with undiluted vaccine survived an intracerebral challenge dose of active MEF 1 virus, compared with only 5% of the non-immunized controls. In the monkeys, although the response to immunization was variable, antibody was developed against all three types of virus.

In the human subjects the antibody titre against at least one component of the vaccine increased in every case, but in 2 instances immunization produced no antibody response against the Type-3 virus. All the subjects who had had antibody against a particular type of virus before immunization showed a rapid and marked rise in the titre after the first injection of vaccine, while 5 out of 7 subjects with no initially detectable antibody against Type-2 virus developed antibody after the first injection, suggesting that they had been previously sensitized to the antigen. The human subjects could be divided into three main groups according to the antibody

titres in the preliminary serum specimens: (1) those with no detectable antibody against any type (3 subjects); (2) those with antibody against only one or two of the three types (8 subjects); and (3) those with antibody against all the virus types (4 subjects). It was noted that the response of the subjects in Group 2 to antigens against which they had no antibody initially was accelerated in comparison with the response of those in Group 1. It is suggested that this may indicate that previous experience of one virus type may sensitize the antibody-production mechanism for heterologous types. *A. Ackroyd*

307. **Specific Serological Reactions in Infective Hepatitis (Botkin's Disease).** (Попытки использования специфических серологических реакций при болезни Боткина)

V. A. Anan'ev and S. V. Lokhova. *Советская Медицина* [*Sovetsk. Med.*] 59–64, No. 12, Dec., 1955.

In an investigation carried out at the Institute of Virology (Academy of Medical Sciences), Moscow, an attempt was made to identify a specific serological reaction in infective hepatitis by studying the complement-fixation and haemagglutination reactions, antigens being prepared from the organs of 5 patients who had succumbed to this disease. The best and most specific results were obtained with antigens from the spleen. Antigen for the complement-fixation reaction was prepared by freezing and thawing, repeated 5 times, and subsequent centrifugation at 3,000 r.p.m. for 30 minutes, the supernatant being used in a dilution of 1 in 40. The antigen for the haemagglutination reaction was a 10% suspension of the organ being tested, after preliminary centrifugation at 1,500 r.p.m. for 5 to 10 minutes.

It was shown that the haemagglutination reaction was inhibited by the serum of patients suffering from infective hepatitis, whereas serum from healthy subjects did not inhibit the reaction provided the serum had previously been passed through a Seitz filter to remove the non-specific inhibitors. It is stated that haemagglutination-inhibiting antibodies accumulate during the early stages of the disease, whereas complement-fixing antibodies do so mainly during convalescence. *A. Swan*

308. **Pattern of 39,500 Serologic Tests in Coccidioidomycosis**

C. E. Smith, M. T. Saito, and S. A. Simons. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 546–552, Feb. 18, 1956. 4 figs., 14 refs.

A total of 39,500 serological tests have been performed at the School of Public Health, University of California, in the diagnosis of coccidioidomycosis. The details of the techniques and the results of the first 21,000 tests have already been published (*Amer. J. Hyg.*, 1950, **52**, 1; *Abstracts of World Medicine*, 1951, **9**, 44). In the present paper the authors report the results of a further 18,500 tests and draw conclusions from the whole series. The findings with both the complement-fixation and precipitin tests show that there is no cross-reaction with viral, bacterial, or spirochaetal infections, nor with the superficial mycoses, actinomycosis, or cryptococcosis. Occasional inconsistent cross-reactions occur, however, in cases of histoplasmosis and blastomycosis.

The value of the tests in detecting coccidioidomycosis depends on the stage of the disease. The results of the tests are positive in only 7% of cases of primary asymptomatic infection, but they are positive in over 90% of patients in whom symptoms are so severe that hospital treatment is necessary. However, asymptomatic pulmonary lesions may often remain at the site of original coccidioidal pneumonitis after the diagnostic antibodies have disappeared. The results of both tests are positive in nearly all cases with extrapulmonary disseminated lesions.

Precipitins appear in the serum earlier than the complement-fixing antibodies, but do not persist so long. Precipitin tests are of limited value in diagnosis 5 months after infection is acquired. The titre of complement-fixing antibody rises with the severity of the infection, and at levels of 1 in 16 to 1 in 32 indicates the probability of dissemination; conversely, regression of the titre is a good prognostic sign. Complement-fixing antibodies appear in the cerebrospinal fluid if meningitis develops, the reaction to the test being positive in 75% of patients with coccidioidal meningitis. *R. B. Lucas*

309. **The Use of the "Differential Test" in the Diagnosis of Infectious Mononucleosis.** (Emploi du "test différentiel" dans le diagnostic de la mononucléose infectieuse)

I. Davidsohn and P. François. *Revue d'hématologie* [*Rev. Hémat.*] **10**, 647–656, 1955. 27 refs.

The authors recall that the test described by Paul and Bunnell for infective mononucleosis is now known not to be specific, but a positive result is strongly presumptive: that is, a titre of 1 in 224 is indicative of infective mononucleosis provided this is confirmed by the clinical and haematological picture.

In other cases in which the titre is high, however, or if there has been a recent injection of horse serum, they recommend that the differential test developed at the Chicago Medical School and Hospital should be carried out. In this test the inactivated serum is first absorbed with a 20% suspension of guinea-pig kidney or a 2% suspension of horse kidney. (Parallel tests performed with these two antigens on 63 samples of serum—34 from cases of infective mononucleosis—gave almost identical results.) The serum is also absorbed with bovine erythrocytes. In each case 1 ml. of antigen is mixed with 0·2 ml. of serum, the mixture allowed to stand for 3 minutes, and the supernatant removed after centrifugation at 1,500 r.p.m. for 10 minutes. The supernatant is then doubly diluted with saline, and aliquots of 0·25 ml. treated with 0·1 ml. of sheep erythrocytes. The tubes are left at room temperature for 2 hours, after which they are inspected for signs of agglutination. The test is diagnostic if at least 1/8th of the activity remains after kidney absorption. There should be a low or zero titre following absorption with bovine erythrocytes. The reaction may be negative in the initial stages of the disease but become positive in 3 to 7 days.

M. Lubran

Pharmacology

310. Clinical Trial of "Doriden", a New Hypnotic. With Note on Use of Ranking Methods in Assessing Therapeutic Effect

M. Rushbrooke, E. S. B. Wilson, J. D. Acland, and G. M. Wilson. *British Medical Journal* [*Brit. med. J.*] **1**, 139–142, Jan. 21, 1956. 6 refs.

The authors report, from the University of Sheffield, the results of a trial in which 18 patients were given α-phenyl-α-ethyl glutarimide ("doriden") in a dose of 0·5 g., cyclobarbitone in a dose of 0·2 g., and an inert placebo to take at night in their own homes for the relief of insomnia. The three types of tablet were indistinguishable in appearance and taste, and were allocated at random so that an equal number of patients received the preparations in the six possible orders. Each drug was taken on 3 successive nights and the patients recorded the time interval between ingestion and falling asleep, the duration and quality of sleep, and the incidence of side-effects if any.

In placing the drugs in order of preference 10 (56%) of the patients put "doriden" first, 6 (33%) put cyclobarbitone first, while 14 (78%) put the placebo in third place, indicating a highly significant measure of agreement among the patients. The average time between taking the drugs and getting to sleep was 71±8·5 minutes with "doriden", 84±10·7 minutes with cyclobarbitone, and 138±20·8 minutes with the placebo. Morning drowsiness was noted on 4 occasions after "doriden" and on 7 occasions after cyclobarbitone—these figures not being significant; one patient experienced nausea on the three mornings after taking "doriden". When "doriden" was given to a further 30 subjects as a hypnotic a widespread erythematous rash appeared on 2 and mental confusion and excitement developed in another.

The authors add an appendix on the principles of ranking methods in clinical trials involving subjective assessment [for details of which the original paper should be consulted]. *T. J. Thomson*

311. Further Experience with Amiphenazole and Morphine in Intractable Pain

J. McKeogh and F. H. Shaw. *British Medical Journal* [*Brit. med. J.*] **1**, 142–144, Jan. 21, 1956. 2 refs.

In a previous paper Shaw and Shulman (*Brit. med. J* 1955, **1**, 1367; *Abstracts of World Medicine*, 1955, **18**, 363) described the value of diamino-phenylthiazole (amiphenazole, DAPT) given together with morphine in the treatment of intractable pain. In the present paper from the University and Austin Hospital, Melbourne, the results in a further 127 cases of intractable pain due to advanced carcinoma are reported. Initially the amiphenazole is given intramuscularly in a dose of 20 to 30 mg. combined with the dose of morphine required to relieve pain—up to 3 grains (195 mg.) in severe cases—in a single injection until the patient is "stabilized", that is until analgesia is complete for 6 to 8 hours; after this (usually in about 2 days) the amiphenazole may be given orally. Large doses of morphine are recommended, the psychological advantage of not allowing the pain to return being stressed. The dose of amiphenazole should be reduced near bed-time.

The authors consider that amiphenazole counteracts the respiratory depression, vomiting, narcosis, depression of the cough reflex, and constipation caused by morphine without affecting its effect on pain. There was no evidence of tolerance or addiction to morphine over a period of 6 months of such medication in any of the present patients. A notable feature was the brightening of the mental outlook observed in 75% of patients receiving amiphenazole. Details of 3 typical case histories are given. *T. J. Thomson*

312. Cardiovascular Actions of Chlorpromazine with Particular Reference to Peripheral Vascular Disease

R. S. Duff, J. W. R. McIntyre, and N. G. P. Butler. *British Medical Journal* [*Brit. med. J.*] **1**, 264–266, Feb. 4, 1956. 4 figs., 5 refs.

The effect of the intravenous infusion of chlorpromazine (in doses up to 45 mg.) on the peripheral circulation in healthy subjects and in patients with vascular disease of the extremities was studied at St. Bartholomew's Hospital, London, by means of venous occlusion plethysmography. In healthy limbs there was an increase of almost 300% in the blood flow in the cutaneous vessels, whereas there was little or no increase in patients with severe arteriosclerosis, Buerger's disease, or Raynaud's disease. In one subject with right femoral arterial thrombosis but otherwise healthy vessels vasodilatation occurred in both feet, although to a lesser extent in the right foot. Of 4 patients with mainly lower-limb disease the circulation through the muscle vessels of the forearm was augmented in 3, but not in one who had advanced Buerger's disease. In all cases the heart rate, after initial fluctuation, was slightly increased and there was a slight fall of blood pressure. The electrocardiogram was unaffected, but the body (oral) temperature fell by 0·5° to 1·5° F. (0·3° to 0·9° C.), this being accompanied by an increased skin temperature. The authors suggest that chlorpromazine might be used in the treatment of arterial embolism or thrombosis, and also as a preoperative method of determining the degree of benefit to be expected from surgical sympathectomy. *I. Ansell*

313. An Evaluation of a New Anticoagulant, Acenocoumarin (Sintrom)

M. Weiner, M. Jiminez, and I. Katzka. *Circulation* [*Circulation* (*N.Y.*)] **13**, 400–403, March, 1956. 1 fig., 12 refs.

Chemotherapy

314. **The Clinical Use of Erythromycin**
S. SOLOMON and B. JOHNSTON. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **230**, 660–674, Dec., 1955. 6 figs., 10 refs.

Experience with erythromycin in the treatment of various infections over an 11-month period at the Bellevue Hospital, New York, is reviewed. Of 122 patients receiving the drug in a dosage of 400 mg. 6-hourly, 88 had pneumonia, 20 other respiratory infections, and 14 suffered from miscellaneous infections. There were 4 deaths among the patients with pneumonia, but only one of these was considered to be due to the pneumonia after adequate treatment with erythromycin. Of the 20 patients with respiratory infections other than pneumonia, only one—with otitis media due to *Alcaligenes faecalis*—failed to recover promptly, while all those with miscellaneous infections responded to treatment with erythromycin. The drug was well tolerated and toxic reactions were few, although in one case treatment had to be stopped because of side-effects.

I. A. B. Cathie

315. **Serum Concentrations and Urinary Excretion following Oral Administration of Penicillin V and Comparison with Penicillin G**
W. W. WRIGHT, A. KIRSHBAUM, B. ARRET, L. E. PUTNAM, and H. WELCH. *Antibiotic Medicine* [*Antibiot. Med.*] 1, 490–495, Sept., 1955. 2 figs., 5 refs.

At the Food and Drug Administration laboratories, Washington, D.C., the authors have compared the antibacterial efficacy of " penicillin V acid " (phenoxymethylpenicillin) with that of benzylpenicillin against 405 strains of *Staphylococcus aureus*. The two drugs were found to be equally effective against 206 of the strains, but the former had a greater activity than the latter against 161 of them, this superiority being most evident against the penicillin-sensitive strains, 123 of which were inhibited by a lower concentration of phenoxymethylpenicillin than of benzylpenicillin; the reverse was true for only 20 strains.

Microbiological plate assays showed that (1) with 1% phosphate buffer (*p*H 6·0) as the solvent, phenoxymethylpenicillin was more active than benzylpenicillin against *Staph. aureus*, but was less active than the latter against *Sarcina lutea*; (2) with pooled normal human serum as solvent, benzylpenicillin was more active than phenoxymethylpenicillin against both organisms, but to different degrees. The theoretical molecular potency of pure phenoxymethylpenicillin was calculated as 1,695 units per mg. and was shown by iodometric chemical assay to be so in fact.

By means of the plate assay method, with *S. lutea*, the serum and urine concentrations of the two drugs were determined in 30 healthy male subjects at 1, 2, 4, 6, and 8 hours after ingestion of 200,000 units of each antibiotic by mouth. The serum concentration of phenoxymethylpenicillin was found in general to be higher than that of benzylpenicillin. Following ingestion of the former drug the proportions of men showing penicillinaemia and the range of the serum concentrations in units per ml. (in parentheses) were as follows: at 1 hour, 76·7% (0·05 to 4·1); at 2 hours, 96·7% (0·086 to 1·7); at 4 hours, 93·3% (0·074 to 0·88); at 6 hours, 66·7% (0·054 to 0·442); and at 8 hours, 20·0% (0·068 to 0·27). The corresponding figures for benzylpenicillin were: at 1 hour, 100% (0·071 to 1·75); at 2 hours, 100% (0·055 to 1·14); at 4 hours, 93·1% (0·01 to 0·32); at 6 hours 58·6% (0·01 to 0·068); and at 8 hours, 10·4% (0·01 to 0·017). In the case of phenoxymethylpenicillin 23% of the subjects had no measurable serum concentration of the antibiotic after one hour, although the drug was present in at least three subsequent serum samples taken from each of the 7 men concerned. Urinary estimations showed that twice as much phenoxymethylpenicillin as benzylpenicillin was excreted in an active form, a fact which the authors attribute to the over-all superiority in stability and material conservation of the former drug.

Joyce Wright

316. **Spiramycin. Clinical and Laboratory Studies**
D. G. HUDSON, G. M. YOSHIHARA, and W. M. M. KIRBY. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **97**, 57–61, Jan., 1956. 3 refs.

Spiramycin is an antibiotic isolated in France from a variety of *Streptomyces*. In tests carried out at King County Hospital (University of Washington School of Medicine), Seattle, spiramycin was appreciably less effective than penicillin and erythromycin in inhibiting the growth of β-haemolytic streptococci and pneumococci *in vitro*, but it was bactericidal to 81 out of 84 strains of staphylococci resistant to penicillin and to 11 of 13 strains resistant to erythromycin.

Therapeutic blood levels (1 to 7 μg. per ml.) were obtained in man by the oral administration of 1 g. 6-hourly. The clinical response to this dosage (with an initial dose of 2 g.) for 5 days in 26 out of 29 cases of bacterial pneumonia was rapid and as good as that to be expected with penicillin or erythromycin therapy. In 2 of the remaining cases resolution was delayed (despite the addition of penicillin and chloramphenicol in one), and in the third, which was fatal, the pneumonia was due to Friedländer's bacillus (*Klebsiella pneumoniae*).

J. Robertson Sinton

317. **Bacteremia Owing to Gram-negative Bacilli: Experiences in the Treatment of 137 Patients in a 15-year Period**
J. A. SPITTEL, W. J. MARTIN, and D. R. NICHOLS. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 302–315, Feb., 1956. 22 refs.

Infectious Diseases

318. Notified Acute Encephalitis (Post-infectious), 1950–54

E. T. CONYBEARE. *Monthly Bulletin of the Ministry of Health* [*Monthly Bull. Minist. Hlth (Lond.)*] **15**, 40–50, March, 1956. 7 refs.

Acute encephalitis associated with infectious disease became notifiable in England and Wales in January, 1950, and with the notification additional information was supplied concerning age and sex distribution and clinical characteristics of the disease. In this paper an analysis is presented of 365 cases notified in the 5-year period 1950–4, 118 of which were associated with measles, 53 with chickenpox, and 136 with mumps.

The average proportion of notified cases of measles encephalitis among notified cases of measles during the period was 1 in 17,500, though the figure varied widely from year to year. The number of cases of encephalitis notified varied roughly in parallel with the seasonal variation in the notified incidence of measles. Though the incidence of measles was highest in the age group 1 to 4 years, the number of notified cases of encephalitis was highest in the age group 5 to 9 years, while the proportion of cases of encephalitis among cases of measles was highest in the age group 25 years and over. There was no appreciable difference in the sex incidence. In more than half the cases the onset of encephalitis was between the 2nd and the 6th days after the rash appeared. The commonest symptoms were drowsiness, coma, convulsions, and stiff neck. Of the 118 patients, 20 died. The information collected concerning the subsequent progress of the survivors was not sufficient to be of value in determining the prognosis in such cases. The author points out that the apparent incidence of measles encephalitis as calculated from notified cases is far less than that obtained from other sources, so that almost certainly notification is very incomplete.

Of the 53 patients with encephalitis in association with chickenpox, 43 were under 10 years of age. There was no outstanding difference in the sex distribution. In half the cases symptoms of encephalitis were first seen between the 3rd and 8th days after the rash appeared, the main symptoms being drowsiness, coma, and meningeal irritation. Six of the patients (4 females) died. The details available concerning the survivors suggests that most of them recovered completely. Uncomplicated chickenpox not being notifiable, no data concerning its prevalence are available. However, a seasonal variation in the incidence of encephalitis was noted, which probably reflects the known seasonal incidence of the primary disease.

The incidence of mumps encephalitis was generally highest in the first quarter of each year and lowest in the fourth. It was highest in the age group 5 to 9 years, males being more frequently affected than females; there were no cases in children under 1 year of age. The onset of encephalitis occurred 2 to 8 days after the parotid swelling appeared. The majority of the patients complained of headache and stiff neck. Of the 136 patients, 5 (3 females) died. The prognosis in the survivors appeared to be very good.

[Although this survey contains nothing new it does draw attention to the serious complications of what are regarded unjustifiably as mild illnesses and to the relative paucity of follow-up information concerning these cases. Here the school medical service might be expected to help by examining affected children and collecting statistical evidence.] *I. M. Librach*

319. Chloramphenicol in Paratyphoid A. Observations with a Note on the Clinical Aspects of the Disease

H. A. REIMANN and PANG TJOEY LIAN. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **96**, 777–780, Dec., 1955. 5 figs., 6 refs.

The effect of chloramphenicol in the treatment of paratyphoid-A infection was studied in 52 patients at Djakarta Central Hospital, Indonesia, 53 untreated patients serving as controls. In most cases treatment did not begin until some time between the 5th and 10th days of the illness, and the average duration of the febrile period, excluding relapses, was 16 days (5 days from the start of treatment). Relapse occurred in 9 of the treated patients, 2 of whom died. In the untreated group the average duration of the illness was 23·7 days, not including any relapse. The condition relapsed in 10 patients in this group and one patient died. It is concluded that chloramphenicol is of some value in paratyphoid A infection, but there is no evidence that it lessens the tendency to relapse. It does not interfere with the immune response. *R. Hare*

320. Use of Benzathine Penicillin G in Carriers of Group A Beta-hemolytic Streptococci

T. J. BROOKS and T. I. MOE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 162–165, Jan. 21, 1956. 12 refs.

An investigation of the value of a single injection of benzathine penicillin in the control and prevention of infection with β-haemolytic streptococci was carried out among recruits joining the U.S. Naval Training Center, Bainbridge, Maryland, between October, 1953, and May, 1954. All recruits whose throat swabs on culture yielded haemolytic streptococci were given 600,000 units of benzathine penicillin intramuscularly within 24 hours. Altogether 2,913 throat cultures were positive for haemolytic streptococci, of which 673 were of Group A.

Of the 673 subjects who were found to be harbouring Group-A haemolytic streptococci, 49 were lost to follow-up. In 597 of the remainder the streptococcus was eradicated from the throat for at least 4 weeks after the single injection and in 10 for 2 weeks; only in 17 were further positive cultures obtained within 2 weeks of the

injection. A considerable number of recruits whose throat swabs were negative initially developed infection with the haemolytic streptococcus; thus there would appear to have been plenty of opportunity for some of the subjects to have been re-infected. However, the incidence of clinical streptococcal pharyngitis during the period of the study was very low. Reactions to the injections were few, only 25 out of the 2,913 recruits complaining of side-effects [but since the subjects were not in hospital and no attempt was made to determine the incidence of minor reactions, these 25 men probably represented only those in whom symptoms were severe enough to compel them to report sick].

It is concluded that in the majority of cases a single intramuscular injection of 600,000 units of benzathine penicillin successfully eradicates haemolytic streptococci from the throat and prevents re-infection, and that this may be a suitable method of mass prophylaxis against Group-A haemolytic streptococcal infections.

C. Bruce Perry

321. **Tetracycline in the Treatment of Human Brucellosis**

G. Chávez Max and R. Nava Fuentes. *Antibiotic Medicine* [*Antibiot. Med.*] **2**, 122–123, Feb., 1956. 1 ref.

The authors report, from the National Institute of Social Security, Mexico City, the follow-up results in 18 cases of brucellosis treated with tetracycline, of which 13 were acute, 2 subacute, and 3 chronic. In every case the agglutination titre was high. In 6 cases blood cultures were positive for *Brucella melitensis*, the most common species of this genus found in the area. Tetracycline was given in daily doses of 1·5 to 2 g. over 40 to 45 days. At the time of the report no clinical or bacteriological relapses had occurred during periods of observation ranging from 45 days to 8 months. The results of treatment were similar regardless of the stage of infection when the case was first seen. Generally there was a rise in temperature lasting 48 to 120 hours. No important modifications were noted in the agglutination titres, but all blood cultures for *Brucella* became negative. On the whole the drug was well tolerated, except for mild gastro-intestinal discomfort in 4 cases.

Douglas J. Campbell

322. **The Clinical Aspects and Treatment of Boeck's Sarcoid.** (Zur Klinik und Therapie des Morbus Boeck) O. Buschmann. *Beiträge zur Klinik der Tuberkulose und spezifischen Tuberkulose-Forschung* [*Beitr. Klin. Tuberk.*] **115**, 203–210, 1956. 1 fig., 28 refs.

From the Municipal Hospital, Bremen, the author briefly reports a series of 75 cases of sarcoidosis, of which 13 were confirmed by biopsy examination and one at necropsy, the diagnosis in the remaining cases being made on clinical grounds; the Kveim test was not employed. Of the 75 patients, 46 were under 30 years of age at the time of diagnosis; 27 of them (36%) had no symptoms, 14 (18·6%) only vague general symptoms, 11(14·6%) presented with erythema nodosum, 10 (13·3%) complained of dyspnoea, 7 (9·3%) had ocular symptoms, and 6 (8%) of the patients showed skin manifestations of sarcoid. One of the patients gave a previous history of pulmonary tuberculosis.

Pulmonary involvement was found radiologically in 70 out of 75 patients, but in 27 of these (38·5%) there was bilateral hilar lymph-node enlargement only. In 10 (14·2%) of the 70 cases there was widespread pulmonary fibrosis or massive nodular involvement, while in the remainder there was both hilar enlargement and a mild degree of parenchymatous disease of the lung. Spontaneous improvement was most marked in those with only hilar enlargement or minimal pulmonary involvement, particularly those with fine miliary shadowing. After an average follow-up period of just over 2 years 35 out of 63 patients had shown a greater or lesser degree of maintained improvement without any treatment. The author briefly discusses the use of cortisone in these cases [but reports no useful new observations].

P. Mestitz

323. **Natural Reservoir of *Histoplasma capsulatum***

H. W. Larsh, A. Hinton, and G. C. Cozad. *American Journal of Hygiene* [*Amer. J. Hyg.*] **63**, 18–27, Jan., 1956. 16 refs.

The isolation of *Histoplasma capsulatum* directly from random soil samples by cultural methods on various solid media has usually been unsuccessful but the authors, at the U.S. Communicable Disease Center, Kansas City, have succeeded in mice by the intraperitoneal injection of the centrifuged supernatant of a 1 in 10 suspension of the soil in saline. The mice, which were protected with antibiotics, were killed after 4 weeks and the combined liver, spleen, and adrenal glands macerated, diluted with saline, and plated on one blood–agar and two Sabouraud's agar plates and incubated at 25° C. for at least 30 days. A total of 1,024 samples of soil from 17 States were tested in this way, isolation of *H. capsulatum* being obtained on 47 occasions.

A relative humidity of 100% and a temperature range of 68° to 86° F. (20° to 30° C.) are necessary for the growth of the fungus. These conditions were most nearly approached in the soil found in " closed " sites, that is, generally in buildings occupied by human beings, inside and under farm buildings, chicken houses, " storm cellars ", caves, and silos. The largest number of isolations (22 out of 137 samples, or 16%) was made from soil in chicken houses, and these houses were all in areas in which the adult human population showed high skin sensitivity to histoplasmin. It is noteworthy that from 107 samples collected from chicken houses in use, only 10 isolations of the fungus were made, whereas from 22 samples from unused chicken houses, 11 isolations were made. It is important to note that *H. capsulatum* has not been isolated from chickens, and it proved impossible to infect these birds with the fungus; nor were their faeces infected. Throughout these investigations wild and domesticated animals [species not detailed] were collected and their tissues cultured, but it was concluded that animals were not a reservoir for the fungus. In the authors' opinion soil, and particularly soil containing organic material, is the natural reservoir of *H. capsulatum*.

Kenneth Marsh

Tuberculosis

DIAGNOSIS AND PROPHYLAXIS

324. The Tuberculin Jelly Test without the Use of Flourpaper

C. P. SILVER. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **49**, 299–307, Oct., 1955. 1 fig., 21 refs.

An attempt was made at the Tuberculosis Dispensary of the London Chest Hospital to assess the value of the plain tuberculin jelly test (that is, without previous abrasion of the skin with flourpaper) by comparing its results with those of the Mantoux test in four groups of children: (1) 204 children aged 4 to 16 with untreated active tuberculosis; (2) 196 East London schoolchildren aged 5 to 11; and (3) 200 children aged 10 to 16 years who had previously undergone vaccination with B.C.G. In addition, 56 children under 5 years old at a day nursery, on whom only the jelly test was performed, were studied. The jelly employed contained 60% of old tuberculin, and was applied between the shoulder blades with a strip of control jelly in the customary manner.

The types of reaction to the jelly most commonly observed in Mantoux-positive children were erythema, vesiculation, and oedema, the maximum intensity being reached at 96 hours. In Mantoux-negative children no skin reaction of any kind was observed on inspection after 72 and 96 hours. The sensitivity of the jelly test in children up to the age of 10 years appeared to lie between that of the Mantoux test with 1 unit and that with 10 units of tuberculin. Above this age the sensitivity of the skin appeared to diminish, and there was a higher proportion of negative reactors to the jelly among those who were Mantoux-positive. In Group 3 all the children were Mantoux-positive, whereas 22 of the 137 under 10 years old gave a negative reaction to the jelly test. In contrast, of 78 children under 10 in Group 1, all of whom were Mantoux-positive, only one gave a negative reaction to the jelly test. The jelly was reliable after keeping for 2 years at refrigerator temperature.

John M. Talbot

325. An Experimental Study of the Value of Antituberculous Vaccination with B.C.G. (Considerazioni sperimentali attorno alla validità della vaccinazione antitubercolare con B.C.G.)

A. M. KREBS. *Notiziario dell'Istituto vaccinogeno antitubercolare* [*Notiz. Ist. vaccin. antituberc.*] **5**, 248–262, Oct.–Dec., 1955. 1 fig., 1 ref.

Out of some 2,800 school-children vaccinated with B.C.G. at the Municipal Office of Hygiene in Milan during the 3 years 1949–51, 353 [whose age, sex, and previous reaction to tuberculin are not stated] were followed up for 4 years to assess the efficacy of this method of prophylaxis. Tuberculin-testing was first carried out 40 days after vaccination and was repeated after 6 months and then annually. The response was positive in 97·5% of cases after 6 months, this proportion gradually decreasing to 61·4% after 4 years. The author is of the opinion that re-vaccination should not be undertaken indiscriminately, but should be dependent upon the subject having a negative reaction to tuberculin.

Franz Heimann

326. B.C.G. and Vole Bacillus Vaccines in the Prevention of Tuberculosis in Adolescents

MEDICAL RESEARCH COUNCIL TUBERCULOSIS VACCINES CLINICAL TRIALS COMMITTEE. *British Medical Journal* [*Brit. med. J.*] **1**, 413–427, Feb. 25, 1956. 19 refs.

This is the first (and preliminary) report of an extensive, controlled, clinical investigation carried out by the Tuberculosis Research Unit of the Medical Research Council into the degree and duration of protection afforded by B.C.G. and vole bacillus vaccines to adolescent boys and girls. The investigation was started in September, 1950, and by December, 1952 (after exclusion of cases considered unsuitable for various reasons) some 56,700 voluntary participants aged between 14½ and 15 years attending secondary modern schools in or near North London, Birmingham, and Manchester were included in the survey. After exhaustive preliminary examination and testing these were divided into five groups as follows: (1) those giving a negative reaction to 100 tuberculin units (T.U.) on entry and left unvaccinated (13,300 children); (2) those negative to 100 T.U. on entry and vaccinated with 0·1 ml. of fresh B.C.G. vaccine from the State Serum Institute, Copenhagen (14,100 children)—allocation to Group 1 or 2 was decided by random selection; (3) those negative to 100 T.U. on entry and vaccinated with vole bacillus vaccine (2 mg. of wet bacilli per ml.) prepared at the Lister Instutute, Elstree (6,700 children, all from Manchester or Birmingham); (4) those positive to 3 T.U. on entry and not vaccinated (16,000); and (5) those negative to 3 T.U. but positive to 100 T.U. and not vaccinated (6,600). No further vaccinations were carried out after the trial had begun. Thus of the 56,700 participants, 20,800 (37%) were vaccinated and 35,900 (63%) were not.

An elaborate follow-up system has ensured the continued observation of the great majority of the subjects (over 94%) for a minimum of 2½ years, and assessment of their progress has been checked by independent observers. The results at June, 1955, showed that the annual incidence of tuberculosis in the five groups was as follows: (1) 1·94 per 1,000; (2) 0·37 per 1,000; (3) (Manchester and Birmingham only) 0·44 per 1,000; (4) 1·75 per 1,000; and (5) 0·74 per 1,000. Closer analysis of the last two groups suggested that the higher the sensitivity, the greater the risk; for example, the

morbidity was nearly 3 per 1,000 in children showing a 15-mm. area of induration in their reaction to 3 T.U. on entry. The total number of children considered to have developed tuberculosis after entry—scrupulous and retrospective measures being taken to exclude patients who might have been admitted inadvertently with disease already active—was 165 up to the end of the 2½ years under consideration. These consisted of 104 cases of pulmonary tuberculosis, 36 of tuberculous pleural effusion without evidence of pulmonary involvement, 11 of cervical adenitis, 4 of bone or joint tuberculosis, 3 of tuberculous meningitis, and 7 of other forms. Of these patients (who had now left school) 68% were ill enough to be unable to work for at least 3 months, but none of them died.

An analysis of the relationship between incidence of disease, vaccination, and initial tuberculin sensitivity [for details of which the reader must refer to the original article] is given. In only 5 of the 165 cases (2 of erythema nodosum and 3 of adenitis) was it thought likely that disease could be attributed to vaccination. The interim conclusion of this careful trial (which is still in progress) is that both vaccines afford effective protection, but it is probably still too early to attempt any evaluation of their relative merits.

[The claim in the report that the observed reduction of 35 to 55% in the expected morbidity from tuberculosis in this particular age group during the first 30 months can be attributed to vaccination seems to be soundly based.] *R. J. Matthews*

RESPIRATORY TUBERCULOSIS

327. **Hinconstarch in the Treatment of Pulmonary Tuberculosis. Report on Pilot Investigation**
V. C. Barry, M. L. Conalty, H. E. Counihan, and B. O'Brien. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] 73, 219–228, Feb., 1956. 5 refs.

Hinconstarch is a polymer prepared from periodate-oxidized potato starch with equimolar proportions of isoniazid and *p*-aminobenzalthiosemicarbazone. It is a yellow, amorphous powder, insoluble in water, which is available in gelatin capsules containing 100 or 200 mg. At Meath and St. Laurence's Hospitals, Dublin, this drug was given for 3 months to 12 patients with pulmonary tuberculosis, 6 with moderately-advanced and 6 with far-advanced disease. The ages of the patients (8 males and 4 females) ranged from 13½ to 59 years. At first the dosage was 0·5 g. daily by mouth, but when the drug was found to be well tolerated the dosage was increased, in most cases to 1·2 g. but in a few to 1·6 g. daily. Since other thiosemicarbazones—for example, amithiozone—are known to cause severe toxic reactions such as anorexia, gastro-intestinal pain, and haemolytic crises particular attention was paid to this possibility.

At the end of 3 months the results obtained were considered to be comparable with those achieved with "the best chemotherapeutic agents in present use". All the patients became afebrile and the mean erythrocyte sedimentation rate (Westergren at one hour) fell from 28·7 mm. to 13·3 mm. Improvement was observed in the chest radiographs; cavity closure was noted in 5 and a decrease in cavity size in 4 of the 9 cases in which there were cavities originally. Sputum conversion occurred in 10 cases; in the remaining 2 cases the sputum contained respectively isoniazid-resistant organisms and organisms of decreased susceptibility. The authors consider that even with adequate dosage resistance may still develop, but not early in treatment. Toxic effects were slight and infrequent. Abdominal discomfort of brief duration developed in 2 patients and transient urticaria in one; the results of the indirect Van den Bergh test were above the normal range in 3 cases, but in none of the patients was there clinical evidence of jaundice, anaemia, or liver disease. The appetite remained good and all but one of the patients gained in weight. *Arthur Willcox*

328. **The Treatment of Active Pulmonary Tuberculosis with Short Infusions of PAS Daily or Twice Daily.** (Le traitement de la tuberculose pulmonaire évolutive par les perfusions courtes de PAS quotidiennes et biquotidiennes)
G. Favez, F. Aguet, and A. Bossy. *Schweizerische Zeitschrift für Tuberkulose und Pneumonologie* [*Schweiz. Z. Tuberk.*] 13, 1–33, 1956. 36 figs., bibliography.

The authors describe the results obtained with short intravenous infusions of PAS in 546 cases of tuberculous disease treated between 1951 and 1954 at the Sylvana Clinic, Lausanne. In their experience the types of disease most suitable for this form of treatment are (1) tuberculous pneumonia, (2) diffuse nodular infiltrative disease, (3) solitary isolated cavitation, (4) miliary infiltration, and (5) meningitis. Because of the instability of PAS solutions only freshly prepared solutions were used; the method of preparation is described in detail. Administration was by continuous intravenous drip. During the first week one infusion was given daily (starting between 8 and 9 a.m.), the period of infusion being reduced gradually from 3 hours to 1 hour. During the following week a second infusion was given daily between 4 and 5 p.m. In addition, 1 g. of streptomycin and 500 mg. of isoniazid were given daily. The infusions were continued twice daily (on 6 days of the week) for the first month and once a day for the next 6 months. The administration of streptomycin was reduced to 3 times a week at the 3rd month, and that of isoniazid to 250 mg. at the 7th month, streptomycin being replaced at this juncture by another [unspecified] drug. In many cases treatment was continued for 18 months in all, and strict bed rest was enjoined for the first 4 to 6 months. Reactions following transfusion consisted in flushing of the face, epigastric heaviness, diarrhoea, somnolence, feelings of fatigue, and loss of appetite, but most of the patients were able to tolerate the treatment despite these discomforts. Intravascular thrombosis was rare and could be prevented by the early application of hot fomentations. Between 1952 and 1954 20 cases of jaundice were seen, 19 of which were thought to be viral in origin.

As a result of their observations the authors are convinced that short infusions (up to 1 hour) were superior to longer ones (2 hours and over), and daily infusions to intermittent ones. During treatment the temperature fell, the sputum diminished in amount, and within 3 to 7 weeks nodules and infiltrations disappeared and recent cavities closed. However, dense, solid lesions, apical micronodular infiltrations, and thin-walled cavities in the midst of otherwise radiologically intact parenchyma were resistant to PAS infusions. Speculating on the mode of action of these infusions, the authors suggest that they stimulate the anti-inflammatory action of endogenous cortisone through the pituitary hormone rather than acting directly, and point out that this would explain the efficacy of the infusions in exudative types of the disease. They issue a warning that such infusions are not to be considered specific in themselves and that their administration raises many unsolved problems, such as the advisability of the concomitant use of hormones (cortisone), and the optimum time and place for collapse therapy, especially pneumothorax. "The soil more than the seed", it is stated, still remains the most important factor in the conquest of the disease.

[It is difficult to see what advantages intravenous infusions have over conventional means of administration. In the abstracter's view, the authors have not made out a very convincing case for their use.]

I. M. Librach

329. **Comparison of the Effect of Four Variables in the Antimicrobial Therapy of Pulmonary Tuberculosis. I. Report of the Cooperative Study of the Veterans Administration, Army, and Navy, April, 1949, to January, 1951**

W. B. TUCKER. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **72**, 718–732, Dec., 1955. 27 refs.

An investigation of certain variables in the chemotherapy of pulmonary tuberculosis is reported in which: (1) the effect of streptomycin was compared with that of dihydrostreptomycin; (2) the results of daily administration of streptomycin were compared with those of intermittent administration; and (3) progress at the end of 3 months was compared with that at the end of 4 months. A total of 813 patients whose sputum was positive for tubercle bacilli were divided at random into 3 groups for the purpose. In 79% the disease was far advanced, while in 84% it was "progressive during an observation period of 60 days immediately before treatment started". It was bilateral in 79% and cavernous in 78%. In 19% some chemotherapy had already been given, and in all cases the organisms were sensitive *in vitro* to 10 μg. of streptomycin per ml. It should be noted that approximately three-quarters of the total number of patients received some form of collapse treatment either during or within four months of the cessation of drug therapy.

At first, attempts were made to assess the results from changes in the patient's general condition, weight, and temperature and the bacteriological findings, but with experience reliance was placed chiefly on the changes observed in the chest radiograph and on the "reversal of infectiousness"—that is, sputum conversion. The author's conclusions are as follows: (1) administration of 1 g. of streptomycin twice a week with 12 g. of PAS daily is as effective as 1 g. of streptomycin and 12 g. of PAS daily; (2) the results of combined therapy with 1 g. of either streptomycin or dihydrostreptomycin and 12 g. of PAS daily are slightly better than those obtained with streptomycin or dihydrostreptomycin alone; (3) streptomycin and dihydrostreptomycin are therapeutically equal, although they differ in their respective toxicity for the two branches of the eighth cranial nerve; and (4) the results achieved with PAS and either streptomycin or dihydrostreptomycin given daily for 4 months are superior to those obtained with the same treatment over a period of 3 months. *Kenneth Marsh*

330. **Comparative Efficacy of Three Streptomycin and *para*-Aminosalicylic Acid Regimens of Prolonged Duration in Patients with Previously Untreated Pulmonary Tuberculosis. II. An Account of the Cooperative Investigation of the Veterans Administration, Army, and Navy, February, 1951, to January, 1952**

W. B. TUCKER. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **72**, 733–755, Dec., 1955. 19 figs., 13 refs.

The relative efficacy of three different combinations of streptomycin and PAS in the treatment of pulmonary tuberculosis was studied. A total of 1,491 patients who had not received chemotherapy before were assigned at random to one of three treatment groups in which the dosage of streptomycin was respectively 1 g. daily, 0·5 g. daily, and 1 g. twice a week, 12 g. of PAS being given daily in all three. The numbers in the three groups were 444, 458, and 589 respectively; at the end of 12 months' treatment the numbers were 263, 263, and 341. At the time of the report (about 18 months after the last patient started treatment) 16% of the 1,491 patients were still receiving the original treatment, 47% had completed the planned course, 35% had discontinued treatment for a number of reasons, including drug toxicity or resistance, and 2% had died.

There was no significant difference between the three groups in the average degree of radiological change or incidence of sputum conversion and cavity closure. When the results for the three regimens were combined a definite correlation was observed between the initial extent of the pulmonary disease, as determined by the number and size of tuberculous cavities present, and the outcome, as assessed on the basis of all the above factors, the conclusion being drawn that "the more extensive the disease the less favourable was the outcome". It was noted, however, that the greatest degree of radiological improvement appeared to occur among those patients with more advanced disease. It is suggested that in reporting improvement in such cases undue significance tends to be given to rapid closure of the larger cavities.

The author concludes that the results of treatment with streptomycin and PAS for 18 to 24 months are

slightly, if not significantly, superior to the results of treatment for a period of 12 months, and that the latter are certainly superior to those achieved over periods of 4 or 8 months. *Kenneth Marsh*

331. **Isoniazid, Streptomycin, and *para*-Aminosalicylic Acid Compared as Two-drug Regimens in the Treatment of Pulmonary Tuberculosis among Previously Untreated Patients. III. An Account of the Cooperative Investigation of the Veterans Administration, Army, and Navy, August, 1952, to September, 1954**
W. B. TUCKER and D. G. LIVINGS. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **72**, 756–782, Dec., 1955. 6 figs., 31 refs.

In a further study of the efficacy of various combinations of chemotherapeutic agents in the treatment of pulmonary tuberculosis (see Abstracts 329, 330) 2,187 patients with sputum-positive pulmonary tuberculosis who had not previously received chemotherapy were divided at random into three groups which were treated as follows: (1) 300 mg. of isoniazid daily with 1 g. of streptomycin twice a week; (2) 300 mg. of isoniazid daily with 12 g. of PAS daily; and (3) 1 g. of streptomycin twice a week with 12 g. of PAS daily. Progress was assessed 8, 12, and 18 months after treatment started.

An interesting feature of the results was an apparent inconsistency—namely, that the least "significant" radiological improvement was observed in cases of minimal disease and the most in cases with a single cavity 4 cm. or more in diameter. Further, in cases without cavitation, whereas the frequency of sputum conversion during the period of treatment was highest in those with minimal and lowest in those with far-advanced disease, the degree of "significant" radiological improvement became progressively greater with the extent of the disease. Various reasons are advanced for this, and it is concluded that the assessment of improvement by the interpretation of serial radiographs, as at present practised, is of limited value, and that greater reliance should be placed on more objective methods.

The best results were obtained with the isoniazid–PAS regimen and the poorest with streptomycin and PAS; the results achieved with isoniazid daily and streptomycin twice weekly were slightly less good than those obtained with isoniazid and PAS daily. Race and age did not appear to have any influence on the outcome. The more advanced the disease and the larger the cavitary component at the start of treatment, the less satisfactory were the results. There was evidence to suggest that the minimum duration of treatment should be 12 months and that for most patients a longer period is advisable.

Discussing the emergence of drug-resistant bacilli the authors state that when either isoniazid or PAS is administered daily with streptomycin twice a week "the rates of emergence of resistant strains are comparable with the two regimens. The drug resistance rates with isoniazid daily and streptomycin twice a week are significantly higher than are those with isoniazid and PAS administered daily". *Kenneth Marsh*

332. **The Intrapleural Application of Isoniazid in the Treatment of Primary Serous Pleurisy.** (Intrapleurale Applikation von Isoniazid zur Behandlung der primären tuberkulösen Pleuritis exsudativa)
M. SALIB, M. NAGY EL MEHALLAWY, and S. SHASH *Schweizerische Zeitschrift für Tuberkulose und Pneumologie* [*Schweiz. Z. Tuberk.*] **13**, 67–74, 1956. 7 figs., 9 refs.

From the Demerdash Hospital (Ibrahim University), Cairo, the authors describe 6 cases of tuberculous pleural effusion which were treated by intrapleural instillation of isoniazid, 4 similar cases not so treated serving as controls. In 4 of the treated cases aspiration of as much pleural fluid as possible was followed by a single intrapleural injection of 250 mg. of isoniazid; in the other 2 the fluid was not aspirated but 250 mg. of isoniazid was injected daily, or on alternate days, for 20 days, a daily oral dose of isoniazid (4 mg. per kg. body weight) being given concurrently. The 4 control patients were treated conservatively, except that aspiration of the fluid was carried out in one case and another was treated with streptomycin and PAS.

According to the authors' criteria, which are described, all 6 patients showed general improvement in well-being, 3 gained in weight, and 5 showed considerable improvement in the radiological findings. There was no appreciable change in the erythrocyte sedimentation rate (E.S.R.). The temperature fell to normal in an average of 5 days, and the average stay in hospital was 43 days. The 4 control patients did not show the same degree of appreciable change over the same period, and the E.S.R., weight, and radiological appearances were unchanged; in these cases the stay in hospital averaged 58 days.

Despite the admittedly small number of cases the authors conclude that intrapleural isoniazid is of value in treating tuberculous pleural effusion. They do not regard concomitant oral administration of the drug as necessary, but consider that initial aspiration of as much fluid as possible improves the results and prevents pleural reactions. *I. M. Librach*

333. **The Handling of the Poor Risk Patient with Pulmonary Tuberculosis: Antimicrobial Therapy, Cardio-Pulmonary Function and Surgery**
A. J. KUKRAL, J. B. GROW, G. MIDDLEBROOK, and S. H. DRESSLER. *Diseases of the Chest* [*Dis. Chest*] **29**, 266–276, March, 1956. 8 figs., 21 refs.

334. **Artificial Pneumoperitoneum in the Treatment of Pulmonary Tuberculosis: a Clinical Study**
L. R. CABIRAN and N. GOLDSTEIN. *Diseases of the Chest* [*Dis. Chest*] **29**, 202–214, Feb., 1956. 4 figs., 13 refs.

Over a 6-year period at the Charity Hospital, New Orleans, artificial pneumoperitoneum was induced for pulmonary tuberculosis in a total of 173 patients. In this paper the follow-up results in 90 patients who received treatment for a minimum of 9 months are reported. The cases were grouped according to the type of lesion—predominantly exudative, predominantly fibrotic, or both exudative and fibrotic—and according to the extent of the disease process. In most cases the

pneumoperitoneum was accompanied by crushing of the phrenic nerve on the same side and, in later cases, also by concomitant administration of streptomycin and PAS. The results showed that most of the patients obtained definite benefit from this treatment, with cavity closure.
J. B. Wilson

335. **Pulmonary Resection in Active Cavitary (Open–Positive) Tuberculosis**
R. H. HOLLAND, J. W. BELL, and E. S. WELLES. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **31**, 83–92, Jan., 1956. 3 figs., 7 refs.

Eighty-three resections in 75 patients with residual cavities and positive sputum are reviewed. An attempt is made to correlate the preoperative findings on tubercle bacilli susceptibility with the complications and therapeutic results. In the original treatment-susceptible patient, resection should probably be performed between the third and sixth month of chemotherapy, and, in the re-treatment patient, several months earlier in order to avoid the development of bacterial resistance. Of the three factors, open cavity, positive sputum, and bacterial resistance, we believe the latter to be the most significant in regard to the postresection complications and therapeutic results. Despite the presence of open cavity and positive sputum, we have had excellent surgical results in our susceptible patients, and only fair results in those who were resistant. The addition of viomycin and "terramycin" [oxytetracycline] to the chemotherapy protocol of 9 resistant patients, 6 weeks postoperatively and continued postoperatively, did not seem to alter the end result.—[Authors' summary.]

336. **Current Experience of Pulmonary Resection at the Forlanini Institute.** (L'esperienza attuale dell'Istituto C. Forlanini sull'exeresi polmonare)
N. DI PAOLA. *Rivista della tubercolosi e delle malattie dell'apparato respiratorio* [*Riv. Tuberc.*] **3**, 413–460, Sept.–Oct., 1955 [received Feb., 1956]. 32 figs.

Resection for pulmonary tuberculosis has been widely employed at the Carlo Forlanini Institute, Rome, only since 1953, the delay in its adoption being attributed by the present author to the great success obtained with various medical and surgical collapse measures. The accepted indications for resection are therefore limited, comprising failure of collapse therapy, destruction of a lobe or lung, bronchial stenosis, tuberculomata [the exact indications in these cases are not specified], cavities in the apex of the lower lobe, and destruction of a lung associated with empyema. The importance attached to preoperative respiratory and cardiac functional assessment is stressed [but there is only the scantiest reference to the use of chemotherapy]. Standard surgical and postoperative techniques are used [though the importance of rapid postoperative expansion of the residual lung and the problem of overdistension are not mentioned].

Of a total of 115 patients on whom resection has been performed, 42 underwent pneumonectomy, with successful results in 30; 56 underwent lobectomy, with good results in 48; and 17 underwent segmental resection, with good results in all. Two patients died from cardiac arrest during operation, while 5 died later from cardio-respiratory insufficiency and 7 from broncho-pleural fistula.
Arnold Pines

337. **Decortication of the Lung in Tuberculous Disease**
T. SAVAGE and H. A. FLEMING. *Thorax* [*Thorax*] **10**, 293–308, Dec., 1955. 15 figs., 21 refs.

The authors describe their experience of decortication in 43 cases of pulmonary tuberculosis treated at Sully Hospital, Glamorgan, between September, 1950, and November, 1954. They conclude that, apart from obliterating the empyema space, the operation leads to an improvement in function in many cases, provided adequate attention is given to postoperative care.

Preoperative pulmonary function studies were carried out in most of their cases, and in some the investigations were repeated postoperatively. Tomography was performed in all cases, and bronchoscopy and bronchography in most. Preoperative treatment included intensive physiotherapy and chemotherapy. The operation itself consisted in a standard postero-lateral thoracotomy, with or without rib resection. The authors consider that there is no virtue in removing the empyema intact—in fact when a large collection of fluid is present it is better to open the space deliberately and aspirate the fluid to prevent the risk of flooding the bronchial tree After removal of the pleura, any disease in the lung was dealt with on its own merits. In 8 of their 43 cases segmental resection was carried out, in 4 thoracoplasty, and in one a wedge resection. The resections were performed at the time of decortication, the thoracoplasties some weeks later.

The importance of immediate and complete expansion of the lung after operation is stressed, this being achieved by applying continuous suction (about −30 inches (−76 cm.) Hg) to drainage tubes; this is sufficient to expand the lung and hold it against the chest wall in the face of the most severe leak. The tubes should be removed only when they cease to function and should be re-inserted if there is a persistent pleural space. As soon as possible the patient is placed, lying on the unoperated side, in a special hyperextension plaster cast, made before operation. In this position the mediastinum tends to fall to the opposite side, the diaphragm is carried caudally, and the ribs are spread apart. The patient lies in the cast except for meals for 3 to 6 weeks, until the chest expansion is equal on both sides or has reached its maximum. The cast is then used only for sleeping in for a further 3 to 6 months.

There were no deaths, and the complications which arose in 16 cases responded to appropriate treatment. After a follow-up period of 6 months to 4½ years reactivation of disease has occurred in 2 cases only. Functional assessment, which is not usually carried out until one year after operation, has shown a striking improvement in the majority of cases, this being estimated by means of bronchospirometry in 18 cases and of measurement of maximum breathing capacity and clinical examination in most of the others. The authors stress that the maximum improvement in function may not occur for some months after operation, and have

shown by angiography in a few cases that blood flow through the pulmonary artery, which is poor in the early stages, may increase considerably later on. In most cases there has been a marked radiological improvement.

A. M. Macarthur

EXTRA-RESPIRATORY TUBERCULOSIS

338. Lymph Node Tuberculosis in Neck, Axilla, and Groin

C. W. LESTER and J. M. JONES. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] 73, 229–238, Feb., 1956. 2 figs., 5 refs.

At Bellevue Hospital, New York, 66 patients, mainly adults, with lymph-node tuberculosis have been treated since the advent of chemotherapy, and in this paper the results are reviewed. Cervical lymph nodes were involved in 65 cases and inguinal lymph nodes in one case; in 8 the axillary nodes were also diseased. There was no sign of tuberculosis elsewhere in the body in 36 cases. Pulmonary tuberculosis was present in 25 (active in 18 and inactive in 7) and disseminated tuberculosis in 3, while in 2 there was a superficial tuberculous lesion in the drainage area of the infected lymph nodes.

The swelling in the lymph nodes disappeared in 7 of the 12 cases in which rest and chemotherapy only were prescribed. Surgical excision was carried out in 54 cases; chemotherapy was given in some cases for about 3 weeks before operation and was given in all cases afterwards. There was recurrence of lymph-node infection in 13.

The authors state that chemotherapy is most effective in the phase of acute inflammation, but that it is of little help in the presence of caseous material or cold abscess, for which surgical treatment is necessary. It has, however, made possible the surgical excision of tuberculous lymph nodes in the presence of active tuberculosis elsewhere in the body. As the authors [very pertinently] point out, excision of tuberculous lung tissue is widely practised with success today; it is therefore difficult to understand why such treatment is only hesitantly employed in cases of lymph-node tuberculosis.

Arthur Willcox

339. Tuberculous Miliary Necrosis with Pancytopenia

W. E. MEDD and F. G. J. HAYHOE. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **24**, 351–364, Oct., 1955. 8 figs., 35 refs.

In this paper from St. Thomas's Hospital, London, and the University of Cambridge, 4 cases of pancytopenia in the peripheral blood associated with miliary tuberculosis are described. In 3 of the cases the diagnosis was established only at necropsy; in the fourth case the condition was diagnosed during life by aspiration liver biopsy and responded satisfactorily to treatment with streptomycin and isoniazid. In all cases the bone marrow ranged in cellularity from normal to frankly hypoplastic, with differing degrees of preponderance of primitive cells of the myeloid series, amounting in one case to a picture apparently typical of acute leukaemia. At necropsy direct invasion of the marrow with focal areas of necrosis and miliary tubercles was not a constant feature, but other organs were affected in this way. The histology of the follicles was unusual in all the cases, the majority of the follicles consisting of small caseous areas with little or no surrounding cellular reaction. This, it is suggested, was the result of invasion of susceptible tissues by unusually virulent or by an unusually large number of tubercle bacilli.

In the authors' view it is possible that the leukaemic, myelosclerotic, and pancytopenic blood complications of acute tuberculosis share a similar pathogenetic mechanism, the active principles being the products of the tubercle bacillus acting on over-sensitive haematopoietic tissues.

The empirical treatment with antituberculous drugs of aplastic anaemia of unknown aetiology is discussed.

E. G. Rees

340. Treatment of Renal Tuberculosis with Triple-drug Therapy. Use of a Combination of Streptomycin, Isoniazid, and Sodium Aminosalicylic Acid

J. K. LATTIMER, H. WECHSLER, A. L. SPIRITO, and G. T. WHITTLE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 544–546, Feb. 18, 1956. 2 figs., 4 refs.

In this paper from Columbia University College of Physicians and Surgeons, New York, the authors attempt to assess the relative value of a number of treatment regimens which they have tried in cases of renal tuberculosis over the past 8 years. Altogether four regimens were used—streptomycin alone, isoniazid alone, streptomycin with sodium aminosalicylic acid, and a combination of all three—in highly comparable groups of patients [the total number of patients is not stated]. All the patients had moderately or far-advanced kidney lesions of the cavitary type.

The most effective regimen was a combination of 1 g. of streptomycin twice weekly, 100 mg. of isoniazid three times a day, and 5 g. of sodium aminosalicylic acid three times a day, the drugs being given simultaneously and treatment continued for one year. Of the 20 patients thus treated none relapsed, the urine being negative for *Mycobacterium tuberculosis* when examined one year after treatment was concluded. This regimen has been so successful that it has not been found necessary to remove a tuberculous kidney or portion of such a kidney for the last 3 years. The authors suggest that prolongation of treatment for 18 to 24 months might be even more effective. They state that no new decline in the incidence of renal tuberculosis has been observed, despite the advent of chemotherapy.

Topical application of a new drug "clorpactin 90" (monoxychlorosene, a hypochlorous acid derivative) was effective in cases of tuberculous ulcer of the bladder. Finally, the authors state that immersion of clean cystoscopes in a 10% solution of formaldehyde for 5 minutes has proved an efficient and harmless method of sterilizing instruments contaminated with *Myco. tuberculosis*.

John Taubman

Venereal Diseases

341. **Has the Incubation Period of Gonorrhoea Undergone a Change?** [In English]
A. LODIN. *Acta dermato-venereologica* [*Acta derm.-venereol.* (*Stockh.*)] **35**, 457–462, 1955. 1 fig., 5 refs.

There is some support in recent literature for the view that since the introduction of sulphonamides and penicillin in the treatment of venereal disease the gonococcus has become attenuated and the incubation period of gonorrhoea has become longer. The author, working at Karolinska Institutet and Garnisonssjukhuset, Stockholm, has compared the incubation period of gonorrhoea in 1,120 young males during three different periods: (1) the years 1932 and 1933 when topical treatment was given; (2) the years 1942 and 1943 when sulphonamides were administered as a routine; and (3) the one-year period 1954–5 during which penicillin was given. Up to 1943 the average incubation period was 5 days; in 1954–5 it was 6 days. A scatter diagram shows a uniform peak at 3 days in all the years. Approximately 90% of the subjects became ill within the first 9 days, but whereas formerly the incubation period exceeded 14 days in only 1% of patients it now exceeded 14 days in 6 to 7%. The interval between the appearance of the first symptoms and the time when advice was sought was 1·8 days in 1932 and 3·9 days in 1954–5. This, in conjunction with the longer incubation period, is taken as evidence of the comparative mildness of the early symptoms and the decreased virulence of the gonococcus. Treatment with sulphonamides and with penicillin has possibly been a causative factor in this attenuation.

F. Hillman

342. **Non-specific Urethritis. A Problem of Management Rather than of Repeated Antibiotics**
P. S. KERSHAW and J. G. LINDSAY. *Journal of the Royal Army Medical Corps* [*J. roy. Army med. Cps*] **102**, 56–60, Jan., 1956.

The authors describe the management of 378 previously untreated cases of non-gonococcal urethritis seen at a British military treatment centre in Japan. The treatment consisted in giving 1 g. of streptomycin by injection plus 2 g. of sulphadiazine at once followed by 1 g. every 4 hours to a total of 32 g. A sodium citrate mixture and abundant fluids were also given. At the end of 3 months 70 patients had relapsed, a relapse rate of 18·5%; there was no significant difference in the relapse rate between fresh cases and cases occurring after gonorrhoea. Of the 70 cases of relapse, the cause was considered to be indulgence in alcohol in 22, "manual trauma" in 13, fresh exposure in 3, and unknown in 32. If those due to "known" causes were excluded the relapse rate was only 8·5%. In 75 further cases, divided into three groups each of 25, one group was treated with the regimen described above, one with 5·5 g. of oxytetracycline over 5 days, and the third with 8·5 g. of aureomycin over 5½ days. The failure rates in the three groups were 19, 36, and 25% respectively. The importance is stressed of the patient's avoiding alcohol and of refraining from "milking the urethra" (which apparently patients often do to ascertain if the discharge has ceased). The cooperation of the patient is thus required, and antibiotics alone are not enough.

[If non-gonococcal urethritis is an infectious disease the causes of failure mentioned above must be precipitating rather than actual; relapse can result only if the patient is not in fact cured.] *R. R. Willcox*

343. **The Dangers of Congenital Syphilis and Their Avoidance.** (Gefahren der angeborenen Lues and ihre Verhütung)
J. OEHME. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **81**, 159–161, Feb. 3, 1956. 18 refs.

A total of 66 infants with clinical signs of congenital syphilis were admitted to the Children's Clinic of the University of Leipzig during the period 1949–53. Of the mothers of these children, 18% were known to have syphilis but had received insufficient treatment during pregnancy, 14% received no treatment although they were known to be infected, and the remainder were not treated, either because no blood test had been carried out or because the results of such tests had been wrongly interpreted or had been incorrect as a result of faulty technique. An analysis of the case histories of 1,334 syphilitic mothers, 200 of whom had received no treatment either before or during pregnancy, showed that the best results are to be expected if treatment is given during the second trimester of pregnancy. Altogether 269 of the children of these women were syphilitic, 198 of these being borne by untreated mothers. In contrast, all the 420 women who had been treated during pregnancy gave birth to healthy children who remained healthy while under observation for periods up to 4 years. The remaining 714 women had been treated before, but not during pregnancy.

It is suggested that every woman who has once been infected with syphilis should be given a "prophylactic course" of penicillin (12 mega units) during each subsequent pregnancy, irrespective of the amount of treatment she has already received, of the results of blood tests (32 syphilitic children in the above series were born of seronegative mothers), and of the condition of her previous children. In addition, it is recommended that the children of syphilitic mothers who have not been treated adequately during pregnancy should be given a "preventive" course of penicillin (600,000 units per kg. body weight). The author admits, however, that these recommendations are subject to modification when the results of the treatment of syphilis with penicillin are more fully known. *A. Fessler*

344. **The Demonstration of Antibodies in the Serological Diagnosis of Syphilis.** (Zur Frage des Antikörpernachweises in der serologischen Lues-Diagnostik)
J. POTEL. *Zeitschrift für Immunitätsforschung und experimentelle Therapie* [*Z. ImmunForsch.*] **112**, 393–402, Dec., 1955. 19 refs.

In a study carried out at the University Institute of Hygiene, Halle, sera from 28 patients with proven syphilitic infections, in which such complement-fixation and flocculation reactions as the Meinicke and citachol reactions were positive, were then tested with cardiolipin and pallida antigens. Some were also tested with spirochaetal agglutination antigen and two by means of the treponemal immobilization test. The results of these cross-tests are presented in a series of tables, and details of the techniques used, including absorption tests, are described.

From these studies the author concludes that the pallida reaction, used as a complement-fixation test, and the spirochaetal agglutination reaction demonstrate the same antibodies in serum, but that the cardiolipin reaction—as a special form of the Wassermann reaction—and the pallida reaction show different antibodies. Quantitative differences between the cardiolipin and pallida reactions are therefore to be expected.

R. D. Catterall

345. **Third Generation Syphilis in an Infant with Serotests Indicating Passively Transferred Maternal Reagins.** [In English]
A. SUNDAL and T. M. VOGELSANG. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **45**, 161–169, March, 1956. 3 figs., 8 refs.

346. **Observations on the Sensitivity of the Haemolytic System in Complement-fixation Tests**
H. M. RICE. *Journal of Clinical Pathology* [*J. clin. Path.*] **9**, 66–70, Feb., 1956. 2 figs., 7 refs.

The effect of the age of the sensitized cell suspension on the serum titre determined by the quantitative Whitechapel Wassermann technique has been investigated by the author at Nottingham General Hospital. Three cell suspensions were used: "new", in the preparation of which the sheep-cell–amboceptor mixtures were kept at 37° C. for 30 minutes before use; "old", in the preparation of which the fresh suspensions were left at room temperature for 5 to 6 hours before use; and "split", in the preparation of which, after the addition of amboceptor to cells, the mixtures were kept at 4° C. for 5 to 6 hours and then at 37° C. for 30 minutes before use. "New" suspensions were used for the complement titrations.

Quantitative tests were performed in parallel on 400 sera with "new" and "old" cell suspensions. In 138 cases a higher titre was obtained with "new" cells; in 115 of these the difference was only of one tube, which is within the limits of technical variation, but 23 sera (5·75%) gave titres 4 to 16 times greater with the "new" cells than with the "old". Only 33 sera gave higher titres with "old" cells, and the difference was never greater than one dilution. A comparison of "new" with "split" cell suspensions in parallel tests on 250 sera showed a similar pattern of results, while in simultaneous tests on the same sera with "split" and "old" cell suspensions 57 sera gave higher titres with "split" cells (48 with a one-tube difference and 9 with a 2-tube difference), and 48 sera gave higher titres with "old" than with "split" cells (45 with a one-tube difference and 3 with a 2-tube difference). Higher titres were also obtained with "new" than with "old" cell suspensions in quantitative gonococcal complement-fixation tests. Complement titrations carried out in parallel with "new" and "old" cell suspensions showed that while the titre was not affected, the end-points were not so clear-cut with "old" cells as with "new". Parallel quantitative tests showed that agitation of the suspension during sensitization by bubbling air through it had no effect on the performance of the haemolytic system.

The author concludes that sensitized cell suspensions show an increased susceptibility to lysis after standing, and that to obtain reproducible results in quantitative complement-fixation tests using optimal-proportion techniques it is essential to use a fresh preparation.

A. E. Wilkinson

347. **A Statistical Study of Autodeviation of Complement in the Bordet–Wassermann Reaction.** (Recherches statistiques sur l'autodéviation du complément dans la réaction de Bordet–Wassermann)
G. ADÉ and R. BRUN. *Dermatologica* [*Dermatologica (Basel)*] **111**, 366–381, Dec., 1955. 1 fig., 33 refs.

The authors present an analysis of the anticomplementary (AC) Wassermann reactions observed at the University Dermatological Clinic, Geneva, between July, 1947, and December, 1953. During this period 104,071 sera from various sources were examined according to the "classic" technique [no details given] by the same personnel. Among these, 334 AC sera were found, the over-all incidence being 0·32% and the incidence in different years varying between 0·18 and 0·47%. As it was not practicable to determine the age and sex of every patient whose serum had been tested, the composition of this population was estimated from a sample survey of 1,000 consecutive sera. Similar sample surveys of the patients tested during the years in which the incidence of AC reactions varied most widely showed no significant difference in age or sex distribution between them.

The 334 AC sera came from 273 patients (22 newborn infants, 2 older children, and 249 adults). The incidence of AC reactions in newborn infants was especially high (7·1%), but no opinion is expressed whether this is due to an intrinsic property of such sera or to poor technique in their collection. The incidence in adults over 50 was considerably higher (0·41%) than in adults below this age (0·14%). Sex apparently had no effect on the over-all incidence, but it was noted that AC reactions were predominantly in sera from males in some years and from females in others. The presence of syphilis had a definite effect, 0·3% of non-syphilitic sera giving AC reactions compared with 4% of sera from syphilitics. [The latter figure seems unduly high.]

The number of AC reactions occurring in each batch of sera tested did not appear to be dependent on the particular batches of sheep cells and complement used. Insufficient data were available to evaluate the possible effect of differences in the batch of amboceptor used. Small variations in the temperature at which sera were inactivated did not appear to influence the results.

The incidence of AC reactions among 3,436 specimens of cerebrospinal fluid tested during the period under review was 0·77%. *A. E. Wilkinson*

348. **The Fate of 294 Pregnancies in Syphilitic Women Treated Entirely before Conception.** (Das Schicksal von 294 Graviditäten luetischer, ausschliesslich vor der Konzeption antiluetisch behandelter Mütter)
G. GUMPESBERGER. *Dermatologische Wochenschrift* [*Derm. Wschr.*] **133**, 189–193, 1956. 25 refs.

At the University Dermatological and Venereological Clinic, Vienna, 294 pregnant women who had been treated for syphilis before conception were studied. In 45 cases penicillin was the primary therapeutic agent, and in the remaining 249 arsenic and bismuth only had been used. Of the latter group, 143 patients were considered to have had insufficient treatment—that is, less than 2 courses of combined metallotherapy in the early stages or less than 5 courses in the later ones. Whereas none of the mothers who had been treated with penicillin gave birth to infected infants, 12 of those treated with arsenic and bismuth did so, 2 of whom had been regarded as adequately treated. All those mothers who were seronegative at the time of labour gave birth to healthy infants. *G. W. Csonka*

349. **Congenital Syphilis and Antenatal Prophylaxis in Leipzig in 1947–54.** (Lues connata und pränatale Prophylaxe 1947 bis 1954 in Leipzig)
D. TUTZKE. *Öffentliche Gesundheitsdienst* [*Öff. Gesundh-Dienst*] **17**, 713–720, Feb., 1956. 1 fig., 12 refs.

The author, writing from the Institute of Social Hygiene, University of Leipzig, contends that at the present time special attention should be given to the prophylaxis of congenital syphilis, since this form of the disease must be regarded as one of the potential after-effects of the large number of infections incurred during and immediately after the war. In East Germany all the necessary measures, such as routine blood-testing of all pregnant women and the prophylactic treatment of those with evidence of syphilis can be legally enforced, and ration cards for the additional foods allowed during pregnancy are issued only to women who attend antenatal clinics.

Out of 43,540 pregnant women whose blood was tested during the period 1950–4, 1,107 (2·54%) were found to be infected with syphilis, but on account of the measures taken only 25 of the children borne by these women had signs of congenital syphilis. In the author's opinion the principal reasons why cases of congenital syphilis still occur in spite of these measures are: non-attendance of pregnant mothers at antenatal clinics, errors in interpretation of the results of the blood tests, and false results of these tests arising from errors of technique in their performance. The number of new cases of congenital syphilis, however, is decreasing steadily; for example, 11 such cases were seen in 1950, but only one in 1954. *A. Fessler*

350. **Serological Studies of Yaws in Thailand**
J. M. F. D'MELLO and P. KRAG. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*]**13**, 1003–1040, 1955. 4 figs., 4 refs.

The authors report the results of the V.D.R.L. test in 6,000 untreated and treated cases of yaws in all its stages seen during an anti-yaws campaign in Thailand in 1951–3, and discuss the value of serology in conducting such a mass treatment campaign, basing their conclusions on the serological examination of 3,632 individuals.

In early untreated cases of yaws (Type I) a strong degree of positivity was commonly obtained irrespective of the age of patient, 97·5% of sera giving a positive reaction up to a dilution of 1 in 256. In the next stage (Type II)—manifested by palmar and/or plantar hyperkeratosis—a somewhat lower level of seropositivity was found, 18% of 544 cases giving a negative result. On analysis by age groups it became clear that at this stage of the disease the serological reaction in the younger age groups is invariably positive, and strongly so. Later on, in a number of cases, the disease may " burn out " and the reaction become negative; this group probably also included a proportion of non-yaws cases in which the hyperkeratosis was due to the rough work in the fields. In any case, the hyperkeratosis of yaws is an active progressive lesion with slow regressive tendencies, as is shown by the high reagin levels in the majority of cases. Of the next stage (Type III), manifested by ulcerative lesions, only 84 cases were seen; as 11 of these were seronegative they were considered to be examples of mistaken diagnosis. There were 342 cases of Type IV (bone and joint lesions or pains) and of these 25·7% gave a negative reaction; some of these were probably also cases of " burnt-out " disease and some non-yaws cases. Once again the younger age groups showed the highest positive titres, there being with advancing years a steady decline towards a negative reaction. In the large group of some 1,500 cases of latent yaws (Type V) the reagin level was generally low (as in Type IV).

The serological response to treatment with procaine benzylpenicillin and aluminium monostearate (P.A.M.) showed that high titres may decrease rapidly in the first 6 months, but further decreases were slow. Seronegativity at the end of one year was obtained in only 11·4% of cases, the best response being obtained in cases of Types I, II, and V. Only 0·3% of the cases showed a slight increase in titre one year after treatment, and in the absence of clinical yaws such an increase is within the limits of technical variation of the test. There was little difference between the serological response to two injections at 3 days' interval of either 1·2 mega units or 600,000 units of P.A.M., and that to 1·2 mega units of P.A.M. given as a single injection.

[It is impossible to do justice in an abstract to this extensive study, and interested readers are referred to the original.] *G. W. Csonka*

Tropical Medicine

351. **Intestinal Amebiasis. Incidence, Symptoms, and Treatment with Arsthinol (Balarsen)**
C. H. BROWN, W. F. GEBHART, and A. REICH. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 360–363, Feb. 4, 1956. 16 refs.

At the Cleveland Clinic Foundation, Ohio, during the 3-year period 1950–2 a total of 7,826 stools from patients with gastro-intestinal symptoms were examined. It was found that in the absence of acute intestinal amoebiasis stool examination after a saline purge was as valuable diagnostically as examination of material obtained at proctosigmoidoscopy. Various parasites were present in 11·2% of the specimens, *Entamoeba histolytica* in 2·1%.

A study of 75 patients with intestinal amoebiasis showed that only one-third had symptoms referable to the presence of *E. histolytica*; in the remainder the symptoms appeared to be due to other gastro-intestinal conditions such as peptic ulcer or gall-stones. Diarrhoea was present in 24% only, and a further 9% gave a history of diarrhoea. Of the 20 patients suffering from abdominal colic, only 7 appeared to have active amoebiasis. Blood was present in the stools in 12 instances, but again other causes, such as haemorrhoids, were responsible in at least 4.

To 34 patients with amoebiasis " arsthinol " (" balarsen ") was given in a dosage of " 5 tablets a day for 5 to 7 days ". *E. histolytica* were absent from the stools of 3 of these 34 patients before treatment, but in these 3 there were typical amoebic ulcers in the rectum. Follow-up investigation one to 15 months after completion of treatment revealed regression of ulcers in these 3 cases and complete disappearance of *E. histolytica* in the remainder. Side-effects, consisting in diarrhoea and abdominal colic, were reported by 3 patients. The authors conclude that the presence of *E. histolytica* in the stools does not necessarily indicate clinical amoebiasis and that arsthinol is an effective drug in the treatment of this disease. *W. H. Horner Andrews*

352. **Treatment of Intestinal Amebiasis with Bismuth Glycolyl Arsanilate**
A. MILZER, E. LEVY, and W. SOKNIEWICZ. *Antibiotic Medicine* [*Antibiot. Med.*] **2**, 42–44, Jan., 1956. 6 refs.

The efficacy of bismuth glycollylarsanilate (" milibis ") in the treatment of chronic intestinal amoebiasis was studied in 83 patients at the Michael Reese Hospital, Chicago. The drug was given in a dosage of 0·5 g. three times a day for 8 days, and stools were examined twice a month for 12 to 16 months, an average of 30 specimens of stool being examined from each patient. Direct fresh faecal emulsion in saline and in D'Antoni's iodine solution, zinc sulphate flotation for cysts, and slides of faecal smears fixed in Schaudinn's solution and stained in Mallory's phosphotungstic acid and haematoxylin stain were used in the examination of each stool specimen.

In 70 out of the 83 cases after a single course stools remained negative for an average of 547 days. In 12 of the remaining 13 there was a response to a second course of the drug, stools being negative for 332 days thereafter. Side-reactions, which were mild and did not interfere with treatment, were observed in 25 cases. These results appear to confirm the value of bismuth glycollylarsanilate in the treatment of chronic intestinal amoebiasis. *A. G. Shaper*

353. **Diethylcarbamazine Control of Bancroftian Filariasis. Follow-up of a Field Trial in West Africa**
I. A. MCGREGOR and H. M. GILLES. *British Medical Journal* [*Brit. med. J.*] **1**, 331–332, Feb. 11, 1956. 2 refs.

In 1951 the population of Keneba, a village in the Gambia, was examined and as many as possible of those infected with *Wuchereria bancrofti* were treated with a total of 25 mg. of diethylcarbamazine (" hetrazan ") per kg. body weight and re-examined after 9 months, as previously reported (*Brit. med. J.*, 1952, **2**, 908; *Abstracts of World Medicine*, 1953, **13**, 285). When the present study was carried out in 1954, more than 3 years later, 390 persons were available for re-examination. At all examinations, microfilaria counts were made on samples of 20 c.mm. of nocturnal blood.

Of 122 persons who had been treated in 1951, microfilariae were absent from 79 at the 1951 follow-up and 90 at the 1954 follow-up, representing a recovery rate of 64·7 and 73·8% respectively. Of 46 infected but untreated persons, microfilariae were absent in only 2 in 1954, a recovery rate of 4·3%. In the treated cases the density of microfilaria decreased by 94·2% (1951) and 87·8% (1954), whereas in the untreated cases the density increased by 32% (1954). Of 43 persons still infected in 1951, 9 months after treatment, 28 (65·1%) were free of microfilariae at the 1954 examination. The contrast with the figure of 4·3% for untreated cases is considered to be significant and due mainly to treatment with diethylcarbamazine. Of 222 persons showing no microfilariae in 1951, 11 were found to be infected in 1954; if these are regarded as cases of fresh infection, then the filariasis infection rate in the village over the period of observation would appear to be 4·9%. Lastly, of 79 persons treated and apparently cured in 1951, 17 (21·5%) were found to be infected in 1954. Since this figure is much higher than the apparent infection rate it is probable that in these cases relapse resulted from the survival of adult filariae. The authors suggest that these somewhat paradoxical results may be due to the relative insusceptibility of immature adult worms to diethylcarbamazine, and that their later maturing might account for the reappearance of microfilariae in cases originally cleared, whereas the mature parent worms are either killed at once or at least sterilized by the selective action of the drug on their reproductive organs.
O. D. Standen

Allergy

354. **Allergy to Mould Spores in Britain**
H. A. HYDE, M. RICHARDS, and D. A. WILLIAMS. *British Medical Journal* [*Brit. med. J.*] **1**, 886–890, April 21, 1956. 1 fig., 33 refs.

The importance of mould spores as allergens in asthma was first recognized and studied in the U.S.A. by Feinberg in 1935. He showed that extracts of mould spores gave positive reactions in 28% of patients with respiratory allergy, that the same spores occurred in the air in vast numbers, and that the time of their occurrence could be correlated with the appearance of symptoms in the patient.

The study of the occurrence of mould spores in the air is more difficult than the study of pollens, since their identification from size and shape is not always possible. Culturing is therefore often necessary, but unfortunately the spores of many species will not grow on laboratory media. A survey of airborne mould spores was started by the authors at Cardiff in 1946 and has since been continued and enlarged by Richards but, being based on the exposure of culture plates, has necessarily been confined to culturable moulds. During the 3 years 1951–3 exposure of plates was carried out at 8 stations in Great Britain, namely, at Cambridge, Cardiff, Harpenden, London, Southampton, York, Liverpool, and Edinburgh. Although the moulds identified belonged to nearly 100 genera, "96% of the total catch . . . belonged to one or other of 11 genera only—as follows: *Cladosporium* (*Hormodendrum*) 37·8%, *Pullularia* 10·4%, *Penicillium* 9·1%, *Epicoccum* 3·4%, *Phoma* 3·0%, *Aspergillus* 2·9%, *Botrytis* 2·7%, *Oospora* 2·6%, *Sporotrichum* 2·1%, *Alternaria* 1·0% (plus a possible 1·3% represented by dark but non-sporing colonies), *Candida* 1·6%". Of these, 6—*Cladosporium*, *Pullularia*, *Epicoccum*, *Botrytis*, *Alternaria*, and *Candida*—were found predominantly in summer; 2—*Aspergillus* and *Oospora*—in the winter; and the remaining 3—*Phoma*, *Sporotrichum*, and *Penicillium*—showed no seasonal variation.

At St. David's Hospital, Cardiff, routine skin tests are carried out in cases of asthma by injecting 0·02 ml. of 1:100 dilutions of extracts made from cultures of the principal moulds present in the air. Positive reactions are common, but the diagnosis of mould asthma is made only if the attacks are confined to, or exacerbated in, the season of the particular mould causing a reaction. By these criteria *Cladosporium* asthma occurred in 26 (4%) of 627 patients tested, and 11 of the 26 were sensitive to *Cladosporium* only. When one of these patients inhaled ground-up *Cladosporium* spores through the nose a severe attack of asthma developed in less than one minute, the vital capacity falling from 4,500 to 1,900 ml. A similar test with *Trichothecium* provoked no such attack. Of 638 patients tested, 6 (1%) were diagnosed as suffering from sensitivity to *Alternaria*. Apart from one case of *Botrytis* sensitivity, no other genera were implicated. Patients who were sensitive to specific moulds were treated with a large measure of success by desensitization.

The authors conclude that allergy to mould spores probably accounts for about 5% of all cases of asthma and may well play a subsidiary part in many more.

Kate Maunsell

355. **Spontaneous Pneumothorax and Subcutaneous and Mediastinal Emphysema in the Asthmatic.** (Pneumothorax spontané, emphysèmes médiastinal et sous-cutané chez l'asthmatique)
J. TURIAF, P. MARLAND, and H. MATHIEU. *Presse médicale* [*Presse méd.*] **64**, 125–128, Jan. 25, 1956. 4 figs., bibliography.

Among 2,000 adult asthmatics seen in recent years at the Hôpital Cochin and the Hôpital Bichat, Paris, there were 12 cases of pneumothorax and 3 of mediastinal and subcutaneous emphysema. All except 3 of these patients were males, and their ages ranged from 17 to 65 years.

Chest pain, an increase of dyspnoea, and malaise were common symptoms. Physical signs were often difficult to elicit, while radiography sometimes showed the presence of emphysematous bullae as well as the pneumothorax, which in some cases was localized. Four patients had small pleural effusions, which in 3 cases was eosinophilic. No special treatment was needed, and absorption of the air was complete in one to 6 weeks in most cases, but 2 patients developed a chronic pneumothorax. One patient had 3 recurrences and another 4. One patient, aged 65, died in a severe exacerbation of asthma a few days after the discovery of bilateral pneumothorax. The incidence and pathogenesis of these conditions are discussed.

[A similar paper published elsewhere by the same authors (*Poumon et Cœur*, 1955, **11**, 999) includes brief case reports.] *G. C. R. Morris*

356. **Prednisone in the Treatment of Bronchial Asthma. Comparative Study on the Effect of Cortisone and Prednisone.** [In English]
E. ANDERSSON. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **9**, 297–303, 1955 [received April, 1956]. 8 refs.

Prednisone was given at the University Hospital, Copenhagen, to 15 patients with severe bronchial asthma who were not responding to treatment with cortisone. Of these, 14 obtained relief, 9 becoming free from symptoms.

The dosage of prednisone was 7·5 to 20 mg. daily, the aim being to keep the dosage at a level corresponding to about one-third to one-quarter the dosage of cortisone or hydrocortisone previously given. Water and salt metabolism was not affected during a follow-up period of just over 3 months. *A. W. Frankland*

Nutrition and Metabolism

357. Parenteral Calories from a Synthetic Water Soluble Fat

H. H. LEVEEN. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **102**, 154–160, Feb., 1956. 3 figs., 12 refs.

In view of the increasing use of fat emulsions (in preference to glucose solutions) for intravenous alimentation and the drawbacks of certain of these emulsions which have already been used, the author reports the investigation at Chicago Medical School of aleuritic acid for this purpose. Aleuritic acid is a substituted palmitic acid in which three hydroxy groups occur on the ninth, tenth, and sixteenth carbon atoms. Glucose monoaleuritate is a glucose ester which is freely soluble in water. Neither the free acid nor the ester are surface active. The ester was shown to be readily metabolized by rat liver mitochondria *in vitro*, with a respiratory quotient of 0·815 and a yield of 6·24 Calories per gramme. It appeared to replace oral tripalmitin completely and effectively when given intravenously to rats. It is non-haemolytic, apparently non-toxic, and completely metabolized, and in the author's opinion has obvious possibilities as an effective source of calories in intravenous alimentation. *A. C. Frazer*

358. Inborn Errors of Lipid Metabolism. Clinical, Genetic, and Chemical Aspects

D. ADLERSBERG. *A.M.A. Archives of Pathology* [*A.M.A. Arch. Path.*] **60**, 481–492, Nov., 1955. 2 figs., 38 refs.

The author has studied, at Mount Sinai Hospital, New York, 89 subjects (including 25 patients and 64 members of the families of 20 of them) with idiopathic hyperlipaemia, and 390 subjects (belonging to 77 families) with idiopathic hypercholesterolaemia. The average lipid levels per 100 ml. of serum in the hyperlipaemic group were: total lipids 3,373 mg., total cholesterol 412 mg., esterified cholesterol 260 mg., and phospholipid 420 mg. In all of the 25 patients and in 3 of their close relatives the serum was milky when examined in the fasting state. Xanthelasma of the eyelids was seen in 2 cases (2·2%), xanthoma tendinosum in one, and xanthoma tuberosum in 12 (13·5%). Coronary arterial disease was present in 14 of the patients and in 16 relatives, that is, in 34% of all cases. In the group with idiopathic hypercholesterolaemia the average levels per 100 ml. of serum were: total lipids 1,101 mg., cholesterol 319 mg., esterified cholesterol 231 mg., and phospholipid 314 mg. In this group the serum was clear in the fasting state, but xanthelasma of the eyelids was observed in 88 cases (23%), xanthoma tendinosum in 19 out of 189 "new" cases (10%), and xanthoma tuberosum in 3 out of 189 (1·6%). Coronary arterial disease was present in 43% of all the cases. Study of the families suggests that these two disorders may be closely related, although their clinical manifestations vary considerably. *A. C. Frazer*

359. Blood Lipid Levels as Influenced by Weight Reduction in Men

N. S. MOORE, J. H. FRYER, C. M. YOUNG, and L. A. MAYNARD. *American Journal of Clinical Nutrition* [*Amer. J. clin. Nutr.*] **3**, 397–402, Sept.–Oct., 1955. 1 fig., 5 refs.

At Cornell University, Ithaca, New York, the total lipid, phospholipid, and cholesterol contents of the blood were estimated and compared in two groups of patients undergoing reduction of weight, all blood samples being taken in the fasting state. Group 1 consisted of 12 men aged 31 to 68 (average 42) who received a diet of 1,400 Cal. containing 80 g. of fat daily. Group 2 also contained 12 men, but these were aged 19 to 28 (average 22); in this group the fat content of the diet was 103 g. per day for the first and last 3-week periods of the study and 50 g. per day for the middle 3-week period. All men in both groups lost weight during the trial, but no correlation was observed between weight loss or fat intake and serum lipid levels. The authors confirm the previously observed wide scatter of serum lipid values, not merely within the groups but for individual members of the groups at different times. These results are compared with those in a similar study carried out by the authors on women (*Amer. J. Med.*, 1954, **17**, 348).

R. E. Tunbridge

360. Some Relations between Body Weight, Body Fat, and Calorie Intake

M. I. GROSSMAN and H. S. SLOANE. *American Journal of Clinical Nutrition* [*Amer. J. clin. Nutr.*] **3**, 403–408, Sept.–Oct., 1955. 13 refs.

In the metabolic studies here reported from the U.S. Army Medical Nutrition Laboratory, Denver, Colorado, in which 87 young, healthy, male subjects took part, records were kept of the caloric intake, body weight, body fat, nitrogen output, and exercise undertaken. The body fat was measured by the skin-fold technique using the Brozek–Keys equation. The caloric intake varied from 2,000 to 4,100 Cal. per day in the different studies.

A poor correlation ($r=0·303$, significant at the 5% level) was found between body weight and caloric intake, 35 of the men maintaining a constant weight on a free diet with a maximum intake of 4,100 Cal. When caloric intake was related to body fat it was observed that for a given body weight intake decreased with increasing body fatness. The loss of body weight which occurred when the subjects received a restricted diet showed a significant correlation with the initial body weight, but no such correlation with the initial body fatness. Similarly, the nitrogen excretion during this period was correlated with the initial body weight but not with body fatness. The authors conclude that factors other than body weight and activity are concerned in determining caloric requirements.

R. E. Tunbridge

Gastroenterology

361. Inhibition of Acid-induced Peptic Ulcer Pain by Local Anesthetics

E. R. WOODWARD and H. SCHAPIRO. *Journal of Applied Physiology* [*J. appl. Physiol.*] **8**, 357–360, Jan., 1956. 1 fig., 4 refs.

The authors report, from the University of California Medical Center and Wadsworth General Hospital, Los Angeles, the effect of the application of local analgesics to peptic ulcers after artificial induction of pain with hydrochloric acid in one case of gastric ulcer and 4 of uncomplicated duodenal ulcer in adult male patients. Multilumen tubes were placed in the pyloric antrum and duodenum under fluoroscopic control and changes in gastric and duodenal pressure were recorded on a multichannel recording oscillograph, the *p*H of gastric and duodenal aspirates being determined with a Beckman *p*H meter.

Typical peptic-ulcer pain was produced in each patient following the introduction of N/10 hydrochloric acid in volumes ranging from 30 to 350 ml. After the pain subsided a solution of lignocaine, amethocaine, or cinchocaine was instilled into the region of the ulcer crater and the acid infusion repeated. The pain response to the acid was found to be completely blocked in 3 patients and greatly reduced in the 2 others. The topical application of the analgesics had no effect on the motility patterns. The authors consider that their findings support the hypothesis that the pain of peptic ulcer arises from chemical stimulation of afferent nerves within the ulcerated area. *T. J. Thomson*

362. The Pseudostenotic Syndrome. Observations on Intermittent Dyspepsia with and without Peptic Ulcer

T. CSATO. *British Medical Journal* [*Brit. med. J.*] **1**, 714–716, March 31, 1956. 3 figs., 4 refs.

Observation of 52 patients with so-called ulcer symptoms revealed two forms of dyspepsia. In the first the symptoms, which were attributed to distension of the lower end of the oesophagus, included heartburn and substernal pain and were often evoked by sitting in a hunched-up position. In the second the characteristic symptoms were epigastric fullness, belching, and nausea which began about an hour after ingestion of food and were relieved by vomiting. It is suggested that the symptoms were due to a disturbance of motility, the radiograph showing dilated coils of small intestine which were intermittent and variable and which could be described as " staggered dumping ". With these changes prolapse of the pyloric mucosa into the duodenum was noted, while in the oesophageal type there was invagination of the mucosa at the cardia into the oesophagus. Alterations in the motility of the small intestine and in the mucosal pattern were constantly found in both types of dyspepsia, but were not observed in patients who were free from distension symptoms. This dysfunction was independent of the tone or emptying time of the stomach and was thought to be an irregular action of the muscularis mucosae, possibly related to emotional, dietary, and postural factors.

The author suggests that his findings merit large-scale investigation under hospital conditions.

Thomas Hunt

363. Medical Management of the Obstructive Complications in Peptic Ulcer

E. A. MARSHALL, M. SASS, and H. BROWN. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **102**, 33–37, Jan., 1956. 2 figs.

The procedure adopted by the authors at Huron Road Hospital, East Cleveland, Ohio, for the treatment of the obstructive complications of peptic ulcer by medical means is described. The necessity for adequate and effective sedation and neutralization of acid peptic activity and the importance of combating excessive nocturnal gastric secretion are emphasized and the value and advantages of an unrestricted diet pointed out. The authors use three standard tablets with the following composition: (1) aluminium hydroxide, 0·65 g.; (2) calcium carbonate, 0·5 g., magnesium oxide, 0·25 g., phenobarbitone, 0·16 g., and atropine sulphate, 0·0002 g.; and (3) calcium carbonate, 0·65 g., phenobarbitone, 0·016 g., and atropine sulphate, 0·0002 g.

On diagnosis of obstruction the gastric contents are immediately withdrawn completely by intubation and the tube then withdrawn; if necessary, the serum electrolyte balance is restored by parenteral administration of fluids. During the first 24 hours no oral feeding is permitted, 2 No. 1 tablets being given every half-hour for 16 hours by day and 4 every hour for 8 hours by night, together with one No. 2 and one No. 3 tablet half-hourly by day and hourly by night. From the second day the patient is given an unrestricted (sometimes low-fat) diet and the dosage of drugs reduced to 2 No. 1 tablets every half-hour and one No. 2 tablet every 2 hours for 16 hours during the day, 4 No. 1 tablets and a glass of milk being given at bedtime and again 2 and 4 hours later; No. 3 tablet may be substituted for No. 2 if diarrhoea results. This regimen is continued for 4½ months.

Of a series of 1,500 radiologically positive cases of peptic ulcer, obstruction was present in 201, the ulcer being duodenal in 172, gastric in 21, marginal in 6, and combined gastric and duodenal in 2 cases. All but 7 of the patients were able to eat an unrestricted diet 24 hours after starting treatment. Of these 7 patients, 6 were over 60 years old, with a long history of peptic ulcer associated with persistent gastric retention; in all 7 surgery revealed pancreatic penetration without cicatricial stenosis. Such stenosis was eventually demonstrated in only 6·5% of the 201 cases. Of 143 patients

followed up for varying periods up to 6 years after cessation of therapy, 10 (6·9%) developed recurrent ulcers with obstructive complications and 18 (12·6%) uncomplicated recurrent ulcers 14 to 65 months after stopping treatment. In the remaining 115 cases (80·4%) the ulcers had not recurred at the time of reporting.

The authors consider that in over 90% of cases the obstructive complications of peptic ulcer are due to spasm and chemical irritation and that these cases can readily be distinguished from those of medically refractory (surgical) obstruction. They stress the importance of the early recognition of obstruction and immediate institution of adequate treatment, for even partial pyloric stenosis delays the healing of an ulcer, and recurrence is more frequent in patients with persistent retention.

P. I. Reed

364. **Peptic Ulcer of the Second Part of the Duodenum**
C. W. CLARK. *Annals of Surgery* [*Ann. Surg.*] **143**, 276–279, Feb., 1956. 4 figs., 7 refs.

365. **Peptic Ulcer, Partial Gastrectomy, and Pulmonary Tuberculosis**
P. A. THORN, V. S. BROOKES, and J. A. H. WATERHOUSE. *British Medical Journal* [*Brit. med. J.*] **1**, 603–608, March 17, 1956. 23 refs.

A low body weight before operation rather than the operation itself is apparently a significant factor in the increased incidence of pulmonary tuberculosis among patients with gastric or duodenal ulcer subjected to partial gastrectomy. This is the conclusion drawn from an investigation carried out at the Queen Elizabeth Hospital, Birmingham, among 955 patients who underwent partial gastrectomy for peptic ulcer. The evidence showed that pulmonary tuberculosis developing after partial gastrectomy was related primarily to the presence of severe or long-standing peptic ulceration and only secondarily to the effects of operation. If the chest radiograph and the patient's weight were normal before operation there was no increased risk of pulmonary tuberculosis after operation. *A. Wynn Williams*

366. **The Use of ACTH and Cortisone in Idiopathic Ulcerative Colitis**
E. J. MALTBY, R. C. DICKSON, and P. M. O'SULLIVAN. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **74**, 4–9, Jan. 1, 1956. 4 figs.

The results obtained with ACTH and cortisone in 109 cases of idiopathic ulcerative colitis seen at the Toronto General Hospital and St. Michael's and Sunnybrook Hospitals, Toronto, between 1950 and 1955 are compared with those obtained in 250 cases treated by other means between 1930 and 1950.

Of the latter group of 250 patients, information was available in 1950 concerning 205; 81 (39·5%) had died and only in 7 of these was the cause of death apparently unrelated to the disease. Death was commonly due to peritonitis, but in 5 cases the cause was carcinoma [site unspecified, but presumably the large bowel]. Half of the deaths occurred within 2 years of the onset of the disease; mortality in patients over 50 years of age was 58% compared with 29% in patients under 50. Only 35 patients in the early series had complete relief of signs and symptoms between attacks.

The dosage of ACTH and cortisone in the hormone-treated series varied, but the authors' present practice is to give 20 units of long-acting ACTH daily, or 75 mg. of cortisone or 5 to 10 mg. of prednisone four times a day. About one patient in 4 failed to obtain any significant or lasting benefit from this treatment; in the remainder there was considerable improvement. In 35 there was complete relief of all symptoms and signs, and the appearances on sigmoidoscopy were normal. A further 36 patients continued to have mild symptoms but were able to resume normal activity; in almost half this group, however, the condition subsequently relapsed. The only serious complication of hormone treatment was adrenal insufficiency in one case following bilateral adrenal haemorrhage. *T. D. Kellock*

367. **The Effect of Sodium Glutamate on Hepatic Coma**
L. T. WEBSTER and C. S. DAVIDSON. *Journal of Clinical Investigation* [*J. clin Invest.*] **35**, 191–199, Feb., 1956. 3 figs., 29 refs.

Encouraging results in the treatment of hepatic coma with glutamic acid were first reported by Walshe (*Lancet*, 1953, **1**, 1075; *Abstracts of World Medicine*, 1954, **15**, 35). The present authors have therefore studied the effects of the intravenous infusion of sodium glutamate on 11 patients with cirrhosis of the liver at the City Hospital (Harvard Medical School), Boston. To 8 of the patients who were in coma, " spontaneous " impending coma, or impending coma induced by the administration of ammonium salts, single or multiple infusions containing up to 23 g. of sodium glutamate were given over a 3- to 4-hour period, while the remaining 3 patients, all in coma, received from 103 to 355 g. of sodium glutamate continuously over 17 to 93 hours. All the patients were maintained on a diet of 2,000 to 2,400 Cal. per day, with not more than 66 g. of protein, and sodium intake was restricted to 200 mg. daily. The state of consciousness was assessed daily, sodium glutamate being given when the depth of coma was increasing or when the level of consciousness appeared to be stabilized.

The results indicated that 23 g. of sodium glutamate had little effect on the mental state, tremor, or plasma ammonium concentration in the course of coma or impending coma, and did not prevent the onset or exacerbation of impending coma induced by ammonium salts. The larger quantities of glutamate given in 3 cases produced slight temporary improvement, but death occurred during or soon after administration, although in these cases the blood ammonium level was kept at or near normal during therapy. Electrolyte imbalance was not marked in the first 8 cases, but in the remaining 3 there was hypokalaemic alkalosis. Perhaps because of their rigid criteria the authors felt that these results were discouraging, but they suggest that sodium glutamate may be of more value in cases of hepatic coma precipitated by ammonium salts, high protein diet, or gastrointestinal haemorrhage. *A. G. Shaper*

Cardiovascular System

368. **The Ballistocardiogram in the Diagnosis of Coronary Arterial Disease**
E. G. WADE, R. M. FULTON, and J. MACKINNON. *British Heart Journal* [*Brit. Heart J.*] **18**, 65–77, Jan., 1956. 6 figs., 27 refs.

With a Starr-type bed, undamped and of a natural frequency of 11 c.p.s., ballistocardiograms (BCGs) were recorded at the Manchester Royal Infirmary from 197 patients with clinical evidence of coronary arterial disease and 38 normal control subjects and compared with electrocardiograms (ECGs) taken on the same day. The conclusions of American workers were confirmed in that the BCG generally proved a more sensitive index of coronary disease than the ECG, for of the 197 patients, 37% had a normal ECG and only 19% a normal BCG. All 38 control subjects had normal ECGs, but one had an abnormal BCG. It is pointed out, however, that the two types of record, one mechanical and the other electrical in origin, reflect two different aspects of myocardial function, which are not necessarily both abnormal together; moreover, neither is specifically related to disease of the coronary arteries.

The normal configuration of the BCG, which has four major waves, H, I, J, and K, related to ventricular systole, and three minor waves, L, M, and N, related to diastolic events, is described and illustrated. The commonest abnormality found in coronary disease, whether or not myocardial infarction has occurred, is known as the " M-type " complex and is seen only in expiration in the mildest cases. It is more commonly found during the 3 months following infarction than later, and it may also be seen in records from apparently normal subjects over 60 years of age. The authors conclude that the BCG may provide useful confirmatory evidence of coronary disease, but it is complementary to, and cannot supplant, the ECG. *J. A. Cosh*

369. **Effects of Adrenocorticotropic Hormone on Pulmonary Function in Cor Pulmonale**
K. BRAUN and S. Z. ROSENBERG. *Journal of Allergy* [*J. Allergy*] **27**, 149–158, March, 1956. 1 fig., 12 refs.

Small doses of ACTH were given to 5 patients (aged 35 to 65 years) with severe emphysema and chronic bronchitis at the Rothschild Hadassah University, Jerusalem. In 2 of the patients there was a history of bronchial asthma, while in all the electrocardiogram indicated the presence of right ventricular strain, ventilatory insufficiency, and arterial unsaturation. ACTH was administered daily either by intravenous drip (3 to 10 mg. in 500 ml. of a 5% glucose solution) or intramuscularly as a gel (20 to 40 units), the duration of treatment being 5 to 9 days. In 3 of the patients there was improvement in ventilatory function accompanied by an increase in oxygen saturation; the patients' general condition also improved. *H. Herxheimer*

370. **The Long-term Use of the Oral Diuretic 3-Chloromercuri-2-methoxy-propylurea (Neohydrin) in Ambulatory Patients**
J. M. EVANS and R. A. MASSUMI. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 124–132, Jan., 1956. 23 refs.

The authors report, from the George Washington University School of Medicine, Washington, D.C., the results of a long-term clinical trial of the oral diuretic " neohydrin " on 40 patients, of whom 38 had congestive heart failure (arteriosclerotic, hypertensive, syphilitic, or rheumatic in origin) and 2 had chronic renal disease. Parenteral mercurial diuretics were successfully replaced by neohydrin (given in tablets each equivalent to 10 mg. of mercury) for periods of 8 to 84 weeks (average 38·6 weeks); effective maintenance doses ranged from 2 to 6 tablets a day.

It was observed that weight fluctuations were less than during the parenteral administration of mercurial diuretics [but no figures are given]. Two patients, with poor oral hygiene, developed gingivitis. In 5 cases the diuretic control was unsatisfactory, and in 9 the drug had to be withdrawn because of side-effects (dermatitis, abdominal pain, bloody diarrhoea, and stomatitis) after periods ranging from 3 days to 29 weeks. The authors conclude that neohydrin is an effective and reasonably safe oral diuretic and that its side-effects are less frequent and less severe than those produced by parenteral mercurials. *W. J. H. Butterfield*

371. **Staphylococcal Infection following Cardiac Surgery**
H. A. FLEMING and R. M. E. SEAL. *Thorax* [*Thorax*] **10**, 327–337, Dec., 1955. 6 figs., 21 refs.

The authors draw attention to the incidence of staphylococcal septicaemia and local staphylococcal infections following cardiac surgery and give clinical details of 9 such cases encountered at Sully Hospital, Glamorgan. In 7 the complication followed mitral valvotomy and in 2 ligation of a patent ductus arteriosus. In 3 of the cases the infection was due to the " non-pathogenic ", coagulase-negative variety of staphylococcus. The diagnosis in the early stages may be difficult as this post-operative endocarditis does not produce the usual clinical picture. Five of these patients developed signs of pulmonary infarction which distracted attention from the underlying septicaemia. The 2 cases in which infection occurred after ligation of the ductus arteriosus were diagnosed by the occurrence of haemoptysis and the appearance of a new radiographic shadow at the operation site owing to the development of a false aneurysm. The patient with a localized myocardial abscess, who died suddenly, was previously in apparently good health.

It is suggested that the development of this condition

* CORRECTION - P. 287
WERE COLLECTED FROM FOUR DIFFERENT HOSPITALS —

is due to the opportunity for infection provided by endocardial trauma, and the authors emphasize the fact that endocarditis of this type is frequently caused by coagulase-negative staphylococci which, in normal circumstances, are non-pathogenic. In a study of the staphylococcal population present in an operating theatre and its personnel during the performance of mitral valvotomy it was found that by the time the crucial point of the operation was reached all gloves, suture material, and packs were heavily contaminated. Until techniques are developed to reduce the amount of airborne infection in theatres, the authors suggest that cardiac surgery should continue to be performed under penicillin cover and that all intravenous and intramuscular injections should be carried out with extreme care in these cases. The importance of carrying out blood cultures in cases of cardiac disease which fail to do well postoperatively and of the immediate use of the appropriate antibiotic if the culture is positive is stressed.

A. M. Macarthur

CONGENITAL HEART DISEASE

372. **Patent Ductus Arteriosus with Pulmonary Hypertension**

I. M. Anderson and H. M. T. Coles. *Thorax* [*Thorax*] **10**, 338–347, Dec., 1955. 3 figs., 21 refs.

The authors review the cases of 9 children aged 1 to 6 years who were diagnosed clinically at the Westminster Hospital, London, as having a patent ductus arteriosus with pulmonary hypertension. In all but one case the condition was confirmed by cardiac catheterization or by direct manometry at operation. Catheterization was repeated after ligation of the ductus in 6 cases, in all of which the pulmonary arterial pressure was found to be normal.

The outstanding clinical features in these cases were marked under-development, considerable asymmetrical bulging of the chest wall in the left parasternal region, and evidence of cardiac enlargement, with a collapsing pulse. In most cases the pulmonary second sound was accentuated and split. Various murmurs were heard, the commonest being a loud holosystolic bruit audible over the whole praecordium, but loudest in the pulmonary area.

In all 9 cases the ductus was either ligated or divided and, with the exception of one child who died 4 weeks after operation, all the patients showed striking clinical improvement. The child who died was shown to have had a reversed shunt through the ductus, and at necropsy a severe degree of atherosclerosis in the smaller pulmonary vessels and gross hypertrophy of the main pulmonary trunk were found. There was associated stenosis of the aortic and mitral valves. The authors are of the opinion that the pulmonary hypertension seen in these cases is secondary to the failure of the ductus to close. In none of their cases was there a history of prolonged anoxia at birth, which has been suggested by Harris as a factor causing persistent patency of the ductus arteriosus.

In view of the probably progressive nature of the vascular changes and of the rapid improvement following ligation of the ductus, the importance of early diagnosis and treatment is stressed. The authors consider that cardiac catheterization is indicated whenever well-marked pulmonary arterial dilatation, enlargement of both ventricles, and increased pulsation of the smaller pulmonary vessels are found on fluoroscopy in a child with the clinical features mentioned above. A precise diagnosis made in this way will enable operative treatment of the ductus to be carried out before irreversible changes occur.

A. M. Macarthur

373. **The Surgery of Patent Ductus Arteriosus**

D. H. Waterman, P. C. Samson, and C. P. Bailey. *Diseases of the Chest* [*Dis. Chest*] **29**, 102–108, Jan., 1956. 4 refs.

At the request of the American College of Chest Physicians the authors have collected and analysed the results of 3,896 operations for patent ductus arteriosus performed by 49 surgeons in various parts of the United States and abroad. Of the patients concerned, 2,929 were children and 967 were adults. Of the former, 69·1% were symptom-free before operation, 27·4% showed signs of myocardial insufficiency, and infection was present in 3·5%, whereas only 48·5% of the adults were symptomless, 40·8% having myocardial insufficiency and 10·7% being infected. The generally better preoperative condition of the children indicated by these differences is also reflected in the results of treatment. The operative mortality in the younger group was 2·3% and in the adult group 5·5%, while the result was clinically satisfactory in 98·3% of the survivors in the former and 95·5% of those in the latter group.

Nearly 60% of the surgeons practised division of the ductus, as opposed to ligation. The initial mortality rates were practically identical for both types of operation in both children and adults. The commonest causes of death were haemorrhage (29 patients), and cardiac asystole or ventricular fibrillation (7), out of a total of 45 deaths in hospital. The majority of the collaborating surgeons favoured ductal interruption in the presence of pulmonary hypertension up to a pressure of 90 mm. Hg systolic. For patients in whom there was reversal of the shunt almost all the surgeons considered that operation should not be advised, but a small minority (8) were prepared to explore and determine the effect of temporary occlusion of the duct; if this resulted in a fall in pulmonary arterial pressure, then they considered that the duct should be permanently interrupted, but not otherwise.

A rather surprising finding was the incidence of aneurysms, which among 1,043 cases reported by 17 surgeons was as follows: 8 of the ductus, 35 of the pulmonary artery, and 31 of the aorta—an over-all incidence of 7·1%.

[It is to be regretted that the authors make no mention of recanalization, particularly in relation to the question of ligation or division, since it was on this score that surgical division as opposed to ligation was originally recommended.]

W. P. Cleland

374. **Direct Vision Intracardiac Surgery in Man Using a Simple, Disposable Artificial Oxygenator**
C. W. LILLEHEI, R. A. DEWALL, R. C. READ, H. E. WARDEN, and R. L. VARCO. *Diseases of the Chest* [*Dis. Chest*] **29**, 1–8, Jan., 1956. 1 fig., 5 refs.

The authors describe in simple terms the "bubble oxygenator" which they have developed and used clinically at the Heart Hospital (University of Minnesota), Minneapolis, whereby the patient's blood is efficiently oxygenated extracorporeally. They state that their former cross-circulation technique for open operations on the heart has now been replaced entirely by the new oxygenator. In essence the apparatus (which is clearly illustrated in a photograph) consists of a length of wide-bore plastic tubing in the shape of an inverted U through which blood is slowly pumped, while 100% oxygen is introduced directly into the moving column through a series of hypodermic needles. Frothing is largely eliminated by contact with a potent, non-toxic, silicone anti-foaming agent. As the blood descends to a settling tube on the distal side bubbles of excess oxygen, together with carbon dioxide, rise to the surface and escape. The apparatus is simple and easily replaceable, and it is claimed that contact with the plastic does not damage the blood cells or affect the clotting mechanism as is the case with glass. The patients are given heparin in doses of 1·5 mg. per kg. body weight, and all replacement blood is similarly heparinized. A rate of flow varying from 172 to 600 ml. per minute was obtained in the cases described.

Details are given of 7 patients, all children, on whom open cardiac operation for septal defect was carried out. In these patients the length of time the heart was open varied from 8½ to 18 minutes. In an addendum the authors state that 36 patients aged from 16 weeks to 21 years have since been operated on with the aid of the oxygenator, the maximum "by-pass" time in this group being 50 minutes. *W. P. Cleland*

375. **Pulmonary Stenosis with Intact Ventricular Septum. Correlation of Clinical and Physiologic Data, with Review of Operative Results**
B. K. SILVERMAN, A. S. NADAS, M. H. WITTENBORG, W. T. GOODALE, and R. E. GROSS. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 53–64, Jan., 1956. 16 figs., 28 refs.

A review is presented of 50 cases of pulmonary stenosis admitted to the Children's Medical Center, Boston, in the 5 years 1949–54. Patients with interventricular communications were excluded, but 14 of the 50 appeared to have interatrial communications. The characteristic pulmonary systolic murmur was present in all the cases, with a thrill in 43, and some history of dyspnoea, fatigue, or mild cyanosis in about half. Cardiac catheterization, carried out in 45 cases, revealed a right ventricular pressure of over 100 mm. Hg in 20, and over 200 mm. in 7. The stenosis appeared to be infundibular in only 3 cases. A useful correlation was found between the electrocardiographic tracings and the height of the right ventricular pressure. Where the right ventricular pressure was over 100 mm. Hg the R wave in right-sided chest leads was over 20 mm. in height, or a "P pulmonale" was present, or S–T and T were depressed in the chest leads. Where the pressure was under 100 mm. Hg these electrocardiographic signs were virtually always absent. In 9 cases there were no signs of right ventricular hypertrophy. The radiograph showed enlargement of the right ventricle in the majority of the cases, prominence of the pulmonary artery in 36, and much diminution of the pulmonary vascular shadows in 27, this last usually being associated with high right ventricular pressure.

Of 21 patients on whom valvotomy was performed by Brock's technique, 3 who had had signs of congestive heart failure died during the operation. In 17 of the 18 survivors the clinical results were good. Catheterization a year or two later in 8 cases showed a fall in right ventricular pressure to about one-third or less of the preoperative level.

Discussing the indications for surgery, the authors state that valvotomy should be attempted as a matter of urgency in cases of severe stenosis with a history of congestive failure, and that valvotomy is justified where the right ventricular pressure is over 100 mm. Hg, but is not necessary when the pressure is below this level.
J. A. Cosh

376. **Closure of an Interventricular Communication by Open Operation with Extracorporeal Circulation. First Successful Case to be Reported from France.** (Fermeture d'une communication interventriculaire à cœur ouvert, sous circulation extracorporelle. Premier succès français)
C. DUBOST, —. PIOT, C. LENFANT, J. PASSELECQ, J. GUERY, H. LE BRIGAND, C. WAPLER, P. BLONDEAU, and M. WEISS. *Mémoires de l'Académie de chirurgie* [*Mém. Acad. Chir. (Paris)*] **82**, 207–216, Feb. 22, 1956. 11 figs., 1 ref.

The various techniques which have been devised for the extracorporeal circulation of the blood during operations on the heart are described. In that used by the authors at the Hôpital Marie-Lannelongue, Paris, blood is withdrawn from the superior and inferior venae cavae of the patient, pumped through an oxygenator, and returned to the right subclavian artery. The simple oxygenator, devised by DeWall, consists of a vertical plastic tube in which the blood rises together with a stream of oxygen; after oxygenation it passes to an inclined tube leading to a descending spiral which is arranged so as to allow the foam to separate. A blood flow of about 800 ml. per minute can be obtained, and an arterial filter is included in the system. The pump, which is an electric finger pump, both aspirates and propels the blood.

The method, which is based on that described by Lillehei *et al.* of Minnesota University, has been employed by the authors so far in only 2 cases. In the first, in a boy aged 7 with a large interatrial septal defect and severe congenital abnormality of both the tricuspid and mitral valves, the operation appeared to be entirely successful, but the patient died with anuria 48 hours later from causes unknown. The second patient, a girl of 4½, had an interventricular septal defect with pul-

monary hypertension. A transverse incision was used, with division of the sternum, and the defect, 1·5 cm. in diameter, was closed with five sutures, the heart being open for 20 minutes. The blood pressure returned to normal immediately the cannulae were withdrawn. The child was discharged from hospital 3 weeks later after an uneventful recovery, although a small retrosternal systolic murmur persists. *M. Meredith Brown*

CHRONIC VALVULAR DISEASE

377. **Some Clinical and Physiologic Effects of Mitral Commissurotomy**
J. A. Wood, J. K. Alexander, C. W. Frank, J. R. West, and D. W. Richards. *Circulation* [*Circulation* (*N.Y.*)] **13**, 178–186, Feb., 1956. 11 refs.

On the basis of clinical and laboratory studies carried out on 18 patients before and after undergoing mitral commissurotomy at the Presbyterian Hospital, New York, the authors offer certain conclusions regarding the selection for this operation of patients with mitral valvular disease. It is suggested that patients whose lesion is well compensated, who are in normal sinus rhythm, and have only slight pulmonary hypertension do best. Those with atrial fibrillation, good compensation, and moderate pulmonary hypertension may benefit; but patients with atrial fibrillation, marked pulmonary hypertension, and congestive failure are unlikely to benefit from operation.

The importance of myocardial function in the production of these results is discussed, and cases illustrative of the three types are described. *H. E. Holling*

378. **The Results of Valvotomy for Aortic Stenosis**
C. G. Baker and M. Campbell. *Lancet* [*Lancet*] **1**, 171–175, Jan. 28, 1956. 18 refs.

The operation of aortic valvotomy carries with it the danger of producing incompetence if a calcified and deformed valve is split. This danger should not be so great in the case of congenital stenosis. In this paper the authors discuss the results obtained at Guy's Hospital, London, in 16 patients who had predominant aortic stenosis with a limited degree of incompetence. The patients' average age was 46, though 2 were children with congenital stenosis. The predominant symptoms were cyanotic attacks and anginal pain, both of which occurred in many cases. The size of the heart was not abnormally great and the electrocardiogram showed evidence of marked left ventricular strain. Dyspnoea and cardiac asthma in some cases suggested left ventricular failure.

There were 6 operative deaths. Of the survivors, 5 were greatly improved as a result of the operation and a further 5 obtained considerable benefit, but 2 of these died at a later date. These results in cases of pure aortic stenosis are not so satisfactory as those obtained in cases of associated mitral and aortic disease. But it is noted that many of the patients were operated on at a late stage of their disease. *T. Holmes Sellors*

379. **Surgical Treatment of Acquired Tricuspid Stenosis**
J. T. Chesterman and W. Whitaker. *Thorax* [*Thorax*] **10**, 321–326, Dec., 1955. 5 figs., 13 refs.

Lesions of the tricuspid valve account for 12% of cases of rheumatic valvular disease, and 15% of cases of tricuspid disease have predominantly stenotic lesions. Since, according to Wood (*Brit. med. J.*, 1954, **1**, 1051 and 1113; *Abstracts of World Medicine*, 1954, **16**, 213), 3,000 mitral valvotomies should be carried out annually in Great Britain, the appropriate figure for tricuspid valvotomy should be 50. The present authors, writing from the City General and Royal Hospitals, Sheffield, describe the various clinical, radiological, and electrocardiographic features which are suggestive of tricuspid stenosis. They emphasize, however, that if these features are absent or equivocal the finding of a higher diastolic blood pressure in the right atrium than in the right ventricle on cardiac catheterization is pathognomonic. In patients with sinus rhythm the atrial pulse pressure is abnormally high and is not transmitted to the ventricle.

As both mitral and tricuspid valves are usually involved together it must be decided which valve should be operated upon first. Unless the main disability is due to increased systemic venous pressure with marked congestion of the face and head, the authors prefer to deal with the mitral valve first. Bilateral valvotomy can be performed if necessary through a transverse sternal splitting incision (Brock) or a right thoracotomy (Bailey). When tricuspid valvotomy alone is to be carried out, the authors prefer a right postero-lateral thoracotomy and approach the valve through the atrial wall rather than the appendage, using two Rumel tourniquets to enclose an oblique field. The best and safest place to start the split is not where the three cusps meet, but between the septal and marginal cusps, which lie directly under the finger, the infundibular and septal cusps, which are adjacent to the outflow tract, being left undivided since a split between them may lead to an increase in regurgitation. Of 4 patients so treated, 3 have survived and have done well. *A. M. Macarthur*

DISTURBANCES OF RHYTHM AND CONDUCTION

380. **Atrial Flutter with 1:1 A-V Conduction. Report of Six Cases**
D. Finkelstein, H. Gold, and S. Bellet. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 65–76, Jan., 1956. 6 figs., 32 refs.

The authors describe 6 cases of atrial flutter with 1:1 A-V conduction seen in hospitals in Philadelphia and Chester, Pennsylvania, between 1947 and 1952. In the 2 youngest patients, females aged 16 and 30 years respectively, the heart was clinically normal. One of these died 5 days after the onset of the tachycardia, which was unaffected by various drugs although a year before a similar attack had responded to intravenous administration of quinine. Necropsy revealed some subendocardial haemorrhage and fibrosis, but the cause

of death was not established. Of the remaining 4 patients, aged 46 to 60 years, coronary atheroma was diagnosed in 2, rheumatic heart disease in one, and thyrotoxicosis in one. One of these died from cerebral thrombosis 9 days after normal sinus rhythm had been restored.

The authors emphasize that prolongation of this form of arrhythmia for more than a few hours commonly results in a fall in blood pressure, congestive heart failure, or even ischaemic heart pain. They distinguish this arrhythmia from supraventricular paroxysmal tachycardia by the following points: (1) the atrial rate in the adult ranges from 225 to 370 beats per minute, whereas the rate of paroxysmal tachycardia ranges from 140 to 220 per minute and vagal stimulation usually stops the paroxysm; (2) the electrocardiogram shows no isoelectric base line between flutter waves; and (3) the occurrence on previous occasions of atrial flutter with 2:1 or higher degrees of A-V block. In each of the 6 cases the QRS complex was prolonged during the attack of flutter, presumably because of impaired intraventricular conduction of a temporary nature. Differentiation from paroxysmal ventricular tachycardia is again made on grounds of rate, which in the latter is usually between 130 and 180 per minute.

Digitalis by intravenous injection is the treatment of choice; failing this, quinidine by mouth, or possibly procainamide by intravenous injection may be tried.

J. A. Cosh

381. **Electric Instability of the Heart. The Concept of the Current of Oxygen Differential in Coronary Artery Disease**

B. L. Brofman, D. S. Leighninger, and C. S. Beck. *Circulation* [*Circulation* (*N.Y.*)] **13**, 161–177, Feb., 1956. 6 figs., 33 refs.

In only a small proportion of cases of coronary disease can death be attributed to the degree of myocardial destruction. The authors suggest that in other fatal cases there is a disorder of cardiac mechanism, and that possibly abnormal impulses (an "injury current") originating from the area of ischaemic myocardium give rise to ventricular fibrillation. They then describe experiments designed to study the manner in which an area of ischaemic myocardium may give rise to an injury current. In these the hearts of anaesthetized dogs were exposed, and areas of local myocardial ischaemia were produced by ligation of the coronary vessels; in some experiments the coronary vessel distal to the ligation was perfused with either oxygenated or anoxaemic blood or blood with reduced haemoglobin concentration; in others general myocardial anoxia was induced, either by clamping the animal's trachea or causing the animal to breathe air of low oxygen concentration, and in this case localized areas of myocardium were perfused with normally oxygenated blood. A 4-channel electrocardiograph (ECG) was used to record the indirect and direct ECG tracings.

It was found that in normally oxygenated hearts and hearts uniformly anoxic throughout there was no variation in the resting electric potentials and spontaneous ventricular fibrillation did not occur. However, when an area of myocardium was rendered ischaemic an injury current was produced, rendering the heart electrically unstable, so that the coordinating mechanism was upset. It was noted that this was associated with a difference of oxygen potential at the junction of normal and ischaemic myocardium. Moreover, it was shown that the uniformly anoxic heart was also electrically stable, but if an area was perfused with oxygenated blood a difference of oxygen potential arose at the border of this area and electric instability again developed, with the danger of ventricular fibrillation. The authors suggest that electrical instability of the myocardium due to unequal coronary blood flow may be responsible for the majority of deaths in patients with coronary disease.

H. E. Holling

CORONARY DISEASE AND MYOCARDIAL INFARCTION

382. **Operative Treatment of Disturbances in the Coronary Circulation of the Heart. A Critical Survey.** (Оперативное лечение нарушений венечного кровообращения сердца (Критический обзор))

A. M. Geselevich. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **34**, 14–24, No. 2, Feb., 1956. 45 refs.

The author describes the various operations which have been devised to increase the blood supply of the myocardium in cases of coronary occlusion; these are of six main types.

(1) The creation of adhesions between the epicardium and myocardium (cardio-pericardiopexy); for this purpose sterile magnesium silicate or asbestos powder has been introduced into the pericardial space, while Aminev proposed the use of iodine or 10% silver nitrate. Some benefit results in about half the cases, but there is a high mortality. Other methods involve suture of the pectoral muscle or omentum to the myocardium. Kolesnikov in 1948 performed a successful cardiopneumopexy, and Minkin in 1953 a mediastinocardiopexy. The spleen and the small intestine have also been used as the extracardiac source of blood supply.

(2) Implantation of the internal mammary artery or its branches into the myocardium of the left ventricle, and anastomosis of that artery with the coronary arteries.

(3) Various workers advocate an anastomosis between the aorta and the coronary sinus, thus arterializing the sinus and reversing the direction of blood flow.

(4) Ligation of the internal mammary artery to encourage the development of a collateral circulation through the pericardial branches; or ligation of the coronary sinus or of the great coronary vein.

(5) Fauteux considered it essential to combine the above operation with complete denervation of the left coronary artery. Other and simpler procedures of the same type include stellate ganglionectomy (Leriche and Fontaine), preaortic ganglionectomy (Arnulph), resection of the stellate ganglion together with the fourth dorsal sympathetic ganglion, and resection of the five upper dorsal root ganglia (Lindgren and Olivecrona).

(6) Procaine blockade of the cardio-aortic plexus, or of the paravertebral ganglia, followed by injection of alcohol. The results of this procedure have not been very satisfactory, especially in cases of established cardiac ischaemia.

Summing up, the author states that such operative procedures can be regarded only as palliative. Experimental results do not give grounds for regarding surgical measures to reinforce the blood supply of the heart as physiologically sound. Of the proposed measures, the most valuable is procaine blockade of the cardio-aortic plexus in the early stages of coronary insufficiency. A final solution of the problem of the surgical treatment of coronary insufficiency in its various stages must depend upon the outcome of methodically planned experiments.

(In the discussion which followed this critical survey it was pointed out that the methods of surgical treatment proposed so far are founded on no basic principles. In severe cases of angina of effort in the early or "functional" stage the obvious line of attack should be on the vegetative nervous system, especially on those areas close to the heart. In the stage of focal arteriosclerosis the operation of "recanalization" of the coronary artery through the common carotid may sometimes be possible, as was done by Valdoni in obliterative endarteritis. In aneurysm of the heart surgical treatment is not excluded; this has been undertaken three times in Czechoslovakia by invagination of the aneurysmal sac followed by suture of intercostal muscle to the site of the aneurysm.)

L. Firman-Edwards

383. **The Beck Operations for Coronary Heart Disease**
H. Feil, W. H. Pritchard, H. K. Hellerstein, R. W. Watts, J. C. Hornberger, and H. M. Helfrich. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 271–282, Feb., 1956. 2 figs., 16 refs.

A report is presented on the results obtained at the University Hospitals, Cleveland, Ohio, in 63 patients with coronary arterial disease who were selected by a committee of 3 physicians for treatment by one or other of the two types of operation devised by Beck for the improvement of the myocardial blood supply in such cases. All the operations were performed by Beck under uniform conditions. Most of the patients selected had intractable angina, though some, who had had a previous myocardial infarction, were asymptomatic. In all, 52 (82·5%) were shown to have had an infarction before operation.

Of the 55 patients who were selected for the Beck-II procedure (arterialization of the coronary sinus by connecting it to the aorta by direct anastomosis or a vein graft), the first stage at least of the operation was completed in 49 with an operative mortality of 45% (22 deaths, 9 of which occurred in the first 13 cases). The Beck-I operation (mechanical induction of pericarditis and partial ligation of the coronary sinus) was performed on 8 patients in whom, for various reasons, it was impossible to place a vein graft, without operative death.

The condition of 30 patients who had undergone the Beck-II and of 6 who had undergone the Beck-I operation and who had survived 6 months or longer after operation was evaluated by the same committee 6 months to 5 years (mostly 1 to 3 years) later. In 17 of the former and 2 of the latter (52·8% of 36) the result was classed as excellent (loss of all pain; able to work) or good (relief almost complete; able to work). Thrombosis of the graft occurred in 8 of the patients who had had the Beck-II operation, the result nevertheless being excellent or good in 3. Physiological studies in cases where the graft was patent showed varying degrees of increase in the cardiac output and blood volume, indicating that an increased load had been imposed on the heart by the fistula.

The authors point out that control studies and long-term follow-up are necessary before the value of these operations can be established, and that in the meantime they should be regarded as experimental procedures.

R. G. Rushworth

384. **Electrocardiographic Changes in Infarction of the Papillary Muscles.** Изменения электрокардиограммы при инфаркте сосочковой мышцы)
N. A. Dolgoplosk. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **34**, 41–50, No. 2, Feb., 1956. 9 figs., 3 refs.

A prolonged systolic murmur which is audible at the apex or in the left subaxillary area after cardiac infarction (and which was not previously present) is strongly suggestive of infarction of the papillary muscles—of the posterior muscles in a posterior infarct, or of the anterior muscles if the anterior wall of the ventricle is involved. Not all patients, however, exhibit this sign after such a lesion. In most of these cases a right ventricular preponderance eventually develops, because owing to its diminished blood supply the left ventricle cannot respond by hypertrophy to the mitral incompetence resulting from necrosis of the papillary muscles, and the right ventricle becomes hypertrophied owing to the strain of maintaining the circulation.

The author concludes, therefore, that if the electrocardiogram (ECG) shows evidence of infarction of the anterior or posterior wall of the left ventricle together with a progressive right ventricular preponderance, necrosis of the corresponding papillary muscles may be presumed, even in the absence of a systolic murmur. The prognosis of this condition is grave. (The article is illustrated with 9 ECG records and detailed histories of 7 cases, in 5 of which the involvement of the papillary muscles was proved at necropsy.)

L. Firman-Edwards

385. **An Evaluation of Anticoagulant Therapy in Acute Myocardial Infarction**
A. R. Gilchrist and J. A. Tulloch. *Scottish Medical Journal* [*Scot. med. J.*] **1**, 1–14, Jan., 1956. 3 figs., bibliography.

A review of the literature reveals much divergence of outlook on the place of anticoagulants in the treatment of acute myocardial infarction. Nevertheless, statistics, accumulated from reliable sources, indicate a halving of the anticipated mortality rate in the first six weeks of the illness with a similar reduction in clinical episodes of thromboembolism.

There is less necessity for the intensive use of these drugs in the so-called " good-risk " cases of acute infarction, but unfortunately the accurate determination of the risk in the earliest stages of the illness, when the need for anticoagulants is greatest, presents considerable difficulty. It is suggested that it is probably justifiable to adapt the length of the course of treatment to the severity of the illness on the day of onset. While optimum benefit is likely to be obtained by a 4 weeks' course of treatment in the great majority of patients admitted to hospital, there is a justification for discontinuing anticoagulants earlier in " good-risk " cases, perhaps after a minimum of 10 days of controlled prothrombin times. The results of this policy remain to be determined. The risks of haemorrhage have been greatly exaggerated. With reliable laboratory support and careful clinical supervision, serious bleeding is seldom encountered.

Evidence suggesting that the benefits of anticoagulants are not solely dependent upon their powers to prevent intravascular clotting continues to accumulate. Not enough is known of the metabolic effects of these drugs. Our autopsy experience, based on an analysis of a consecutive series of 248 post-mortem examinations, does not support the claim that anticoagulants are responsible for a significant reduction either in the incidence of intraventricular thrombi or of peripheral arterial infarcts in fatal cases of acute myocardial infarction. On the other hand, it is enlightening to discover a pronounced and highly significant reduction in the incidence of pulmonary infarction in the treated but fatal cases, a finding which emphasises the importance of the peripheral venous system and justifies the employment of these drugs in the first few weeks of the illness.

In brief, a consideration of the available evidence, clinical, experimental and pathological, strengthens the belief that anticoagulants are of value in the treatment of acute myocardial infarction.—[Authors' summary.]

386. **Triethanolamine Trinitrate (Metamine) in the Treatment of Angina Pectoris: A Long-term Study**
E. M. HELLER. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **74**, 197–204, Feb. 1, 1956. 5 refs.

Experience of a new long-acting vasodilator, triethanolamine trinitrate (" metamine "), in the treatment of 26 cases of classic angina pectoris is described. All patients had been under observation for a minimum of 6 months before treatment started, and in all cases the drug was given in a dosage of six 2-mg. tablets daily for the first two weeks, gradually reduced to 1 to 3 tablets daily over the next 6 to 8 weeks. Of the 26 patients, 15 stopped taking the drug because it proved of no benefit. Of the remainder, 3 males and 8 females aged 43 to 68 years, 9 had a proved attack of cardiac infarction before starting treatment. In 4 of the 11 cases there was marked and lasting benefit from metamine, the improvement being noted after the first few days. In one case acute coronary insufficiency developed and the drug had to be discontinued. However, this was not followed by any increase in the number of anginal attacks. In 6 cases there was acute cardiac infarction, which proved fatal in 2, during treatment with metamine. Of the 15 patients who did not persist with metamine, 2 experienced an attack of acute cardiac insufficiency, but none suffered cardiac infarction during the period of observation; 3 died, from acute pulmonary oedema, cerebral haemorrhage, and pneumonia respectively.

In view of these findings the author raises the question whether long-term administration of metamine may not predispose to further cardiac infarction. He considers that this drug and other coronary vasodilators should be the subject of further investigation before its continued administration is advised. *H. F. Reichenfeld*

PERIPHERAL ARTERIES

387. **Dilatal in the Treatment of Intermittent Claudication in the Calf Muscles**
D. N. WALDER. *Lancet* [*Lancet*] **1**, 257–260, Feb. 11, 1956. 3 figs., 8 refs.

" Dilatal " is a new drug which, it is claimed, increases muscle circulation. It was originally synthesized in 1950 by Kulz and Schneider from an adrenaline-like basal substance, *para*hydroxy-ephedrine, to which by substitution a lengthy side-chain was added, resulting in phenyl-*iso*-butyl-nor-*para*hydroxy-ephedrine. In this paper from the University of Durham the author reports a clinical trial of the drug in 26 patients with intermittent claudication, some of whom had not been treated previously, while others had received tolazoline, or had been treated by sympathectomy; 24 matched patients served as controls. There was a statistically significant subjective improvement in the treated patients, but this improvement could not be confirmed by objective tests of blood flow. In some of the patients in an acute clinical trial the drug caused a transient increase of the blood flow in the muscles of the calf. The author concludes that it is necessary to determine by individual clinical tests which patients will respond to dilatal.
Leon Gillis

388. **Treatment of Peripheral Vascular Disease with " Cyclospasmol "**
R. O. GILLHESPY. *Angiology* [*Angiology*] **7**, 27–31, Feb., 1956. 5 refs.

This paper from Dudley Road Hospital, Birmingham, describes the treatment of 36 cases of senile obliterative arterial disease of the legs and 29 cases of Raynaud's disease with trimethyl*cyclo*hexanol mandelate (" cyclospasmol "), the results of which have, on the whole, been most gratifying.

The former group consisted of 29 male patients (average age 59½ years) and 7 females (average age 65½ years). All had well-marked intermittent claudication of at least 3 months' duration, were free from anaemia, and had failed to respond to previous treatment. The dose of cyclospasmol was 100 mg. 3 times a day, and progress was reviewed at monthly intervals. Of these 36 patients, 19 are now able to go about their daily work without experiencing intermittent claudication in

normal circumstances, and 13 have occasional pain only, which has little effect on their daily life; only in 4 cases was there a poor response to the drug.

In the latter group there were 23 females and 6 males, their ages ranging from 14 to 65 years, all of whom had typical Raynaud's disease. They received the same dosage as the former group. In the juvenile type of the disease in women the response to treatment was good; of 14 patients in this category, 5 have been completely relieved of attacks and in 6 the attacks have decreased considerably in frequency and intensity: there was little or no improvement in 3 cases. The results in the senile type of Raynaud's disease in women, however, have been disappointing; although there were only 6 cases in this category, the occurrence of 4 failures suggests that the drug is of little value in this type of case. In the 3 remaining female patients and in the male patients, in whom the disease could not be classified as either juvenile or senile, the results were mostly good, there being only one failure.

The author points out that it will not be possible to assess the full value of this drug until a great many patients have been observed over a long period, but the results so far are encouraging and there is no doubt that cyclospasmol will prove a valuable drug in the treatment of peripheral vascular disease. Cyclospasmol has also been used successfully in a small number of cases of acrocyanosis, chilblains, frostbite, and night cramps.

Leon Gillis

389. **Relations between Diet and Atherosclerosis among a Working Population of Different Ethnic Origins**

F. H. EPSTEIN, R. SIMPSON, and E. P. BOAS. *American Journal of Clinical Nutrition* [*Amer. J. clin. Nutr.*] **4**, 10–19, Jan.–Feb., 1956. Bibliography.

At the Sidney Hillman Health Center, New York, the relation between dietary habits and the incidence of atherosclerosis in 250 working men and 165 women was investigated. More than 85% of the population studied fell into the two main ethnic groups, Jewish and Italian, and the remainder—apart from a few negroes—were mostly natives of north-east Europe. The average age of the men was 57 and of the women 54 years, height 164 and 153 cm., and caloric intake 2,240 and 1,860 Cal. The mean proportion of the caloric intake which was derived from fat was 34·7% for men and 35·9% for women, there being no significant difference between the groups in this respect; 68% of the fat consumed by the Italians was of animal origin compared with 80% of the fat consumed by the Jews.

There was no relation between the weight and the serum cholesterol level either in men or in women. Men whose diet contained 40% or more of fat showed a greater prevalence of hypercholesterolaemia, but women failed to conform to this trend, although the numbers involved were not sufficient to allow any statistical significance to be attached to this difference. Hypercholesterolaemia was significantly more frequent in Jewish men than in Italian men, and there was a similar, though less marked, difference between the women of the two groups. The amount of dietary fat was related to the incidence of aortic atherosclerosis (as indicated by calcification) in men but not in women. In a larger group of men, for whom dietary histories were not available, the frequency of manifest coronary arterial disease was more than twice as high among Jews as among Italians, despite the fact that both groups seemed to have much the same total fat intake. These findings suggest that dietary factors alone do not explain completely the predisposition of Jews to develop hypercholesterolaemia and coronary arterial disease. Obesity by itself did not appear to predispose either to coronary disease or to aortic atherosclerosis.

[There are several interesting and controversial statements in this paper. It is surprising to learn that the mean caloric intake of working men in New York is only 2,240 Cal. and of women 1,860 Cal.]

Z. A. Leitner

SYSTEMIC CIRCULATORY DISORDERS

390. **Occlusion of a Renal Artery as a Cause of Hypertension**

E. F. POUTASSE. *Circulation* [*Circulation (N.Y.)*] **13**, 37–48, Jan., 1956. 5 figs., 47 refs.

It has been shown experimentally that partial compression of a renal artery causes hypertension. In this paper from the Cleveland Clinic Foundation, Ohio, 3 cases of unilateral occlusion of a renal artery associated with renal hypertension are described and the literature is reviewed. The patients, males aged 30, 51, and 52 respectively, had severe, rapidly advancing hypertension, and in all 3 translumbar aortography revealed unilateral obstruction of a renal artery. The hypertension was completely relieved by nephrectomy. The obstruction of the renal artery in these cases appeared to be due to thrombosis. The author states that with proper safeguards translumbar aortography is a safe and relatively simple procedure; it has been carried out at this clinic in some 250 cases without serious complications.

K. G. Lowe

391. **Body Fluids in Hypertension and Mild Heart Failure**

M. WALSER, B. J. DUFFY, and H. W. GRIFFITH. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 858–864, March 10, 1956. 3 figs., 18 refs.

The authors estimated the extracellular fluid volume by means of a solution of sodium sulphate containing radioactive sulphur (^{35}S) injected intravenously and the blood volume by the injection of erythrocytes labelled with radioactive chromium (^{51}Cr) in 32 normal subjects, 11 patients with uncomplicated hypertension, and 24 patients with early congestive heart failure at the U.S. Naval Hospital, Bethesda, Maryland. Half the patients with congestive heart failure had rheumatic heart disease and the rest coronary arterial disease, with or without hypertension; the systemic venous pressure was greater than 90 mm. H_2O in all cases, but there was no obvious oedema.

In the normal subjects the extracellular fluid volume ranged from 11·4 to 19·4 (mean 16·1) litres per 100 kg. body weight, and its ratio to the blood volume from 1·85 to 3·30 (mean 2·61). There was no significant difference between the normal and hypertensive subjects in respect of these values, but in view of the wide range of normal values and the small number of hypertensive subjects studied, this finding is not conclusive. The mean extracellular fluid volumes for the patients with coronary arterial disease and rheumatic heart disease were 21·0 and 23·9 litres per 100 kg. respectively, the value in 17 of these 24 cases exceeding the highest level recorded in a normal subject. There were no significant differences between the three groups in respect of mean blood volume. *K. G. Lowe*

392. **A Comparative Study of the Treatment of Essential Hypertension. The Effect of Rauwolfia and a Rauwolfia Compound (Rauwolfia, Mannitol Hexanitrate, and Rutin)**
S. Stonehill. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **97**, 189–193, Feb., 1956. 8 refs.

The author, at the General Hospital, Rochester, New York, studied the clinical and hypotensive effects of powdered whole root of *Rauwolfia micrantha* given alone and in combination with rutin and with mannitol hexanitrate on 17 ambulant patients who had moderate to severe hypertension. The blind-test technique was used; each patient received one of these drugs or a placebo in the form of identical tablets for a period of 6 months, when, unknown to the patient, a different drug was substituted. The average reduction in systolic and diastolic pressures in both arms with the patient sitting and lying down was recorded. There was some reduction in blood pressure with the placebo, but with rauwolfia a more pronounced effect was obtained which was enhanced when mannitol hexanitrate and rauwolfia were given in combination. *P. Hugh-Jones*

393. **Reserpine–Hydralazine Combination Therapy of Hypertensive Disease, with Hydralazine in Doses Generally below the "Toxic Range"**
R. E. Lee, A. M. Seligmann, D. Goebel, L. A. Fulton, and M. A. Clark. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 456–465, March, 1956. 14 refs.

394 **Action of "Ecolid" in Man**
F. H. Smirk and M. Hamilton. *British Medical Journal* [*Brit. med. J.*] **1**, 319–322, Feb. 11, 1956. 2 figs., 32 refs.

In this report from the University of Otago Medical School, New Zealand, the authors describe their experience with "ecolid", a new ganglion-blocking agent which is chemically different from both hexamethonium and pentolinium, in the treatment of 42 patients with essential hypertension, of whom 19 had previously been treated with pentolinium, while the remaining 23 had had no previous treatment.

In 10 cases in which similar falls of blood pressure were obtained with either ecolid or pentolinium, the effective dose of the latter was found to be from one to 3·6 (mean 2·1) times that of ecolid. In 9 cases it was possible to compare the effective oral dose with the corresponding parenteral dose; the former was found to be about 15 times greater, a higher ratio (up to 28 to 1) being found particularly in cases in which large doses were necessary. The duration of the decrease in blood pressure varied with the amount of the reduction, which was greatest 1 to 2 hours after administration, between 7 and 13 hours. The effect of posture on the level of the blood pressure was similar to that experienced with other ganglion-blocking agents.

Tolerance to ecolid was noted after a few days' treatment, but varied considerably from patient to patient; cross-tolerance with pentolinium was also observed, the initial doses of ecolid necessary in cases which had previously been treated with pentolinium being larger than those in previously untreated cases. The side-effects were similar to those observed with other ganglion-blocking drugs, but some patients found them less severe; on the other hand, some felt better on pentolinium. The authors conclude that ecolid is a useful addition to the range of hypertensive drugs and that it merits further trial. *H. F. Reichenfeld*

395. **Cranial Artery Vasculography and (Extra) cranial Headache**
M. M. Tunis. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **74**, 185–192, Feb. 1, 1956. 6 figs., 15 refs.

Thirty-five hundred vasculographic (extracranial artery pulse wave contours) records were obtained from more than 130 patients with the presenting complaint of daily recurrent cranio-facial pain. The brachial artery blood pressure varied only insignificantly in all these normotensive patients during 3 to 14 months of observation and with administration of the investigated chemical agents. All the patients studied had demonstrable sustained alteration of the contractile state of certain (extra)cranial tissues (skeletal muscle, blood vessels) associated with their daily recurrent headaches.

Dimenhydrinate in intramuscular doses of 50 to 75 mg. terminated the acute headache attacks in 80% of 56 patients in whom vasculographic records gave evidence of dilatation and/or distension of the temporal arteries associated with the temporal head pain. Triethanolamine trinitrate biphosphate (previously referred to as TTB) in oral doses of 2 to 5 mg. was analogously effective in 80% of 80 patients whose vasculographic records gave evidence of temporal artery constriction and temporal muscle contraction headache. A group of 28 headache cases, refractory to the above chemical agents, was characterized by extreme variability on the vasculographic records from day to day. These patients reported marked diminution in the frequency and intensity of their head pain in association with the administration of the dihydrogenated ergot alkaloids. There are diagnostic implications in the foregoing data, although, as is not unusual, exceptions were encountered.

Additional criteria other than the vasculographic data are important in the selection of the appropriate patient for the chemical agent in some instances. Such criteria will be further reported.—[Author's summary.]

Haematology

396. **Hemoglobin H. Clinical, Laboratory, and Genetic Studies of a Family with a Previously Undescribed Hemoglobin**

D. A. RIGAS, R. D. KOLER, and E. E. OSGOOD. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] 47, 51–64, Jan., 1956. 7 figs., 32 refs.

This paper records the finding of a new abnormal haemoglobin, named haemoglobin H, in 3 of 4 siblings of a Chinese family, all of whom were suffering from hypochromic anaemia and splenomegaly. Whereas all other known variants of haemoglobin move on electrophoresis at alkaline *p*H more slowly than haemoglobin A, haemoglobin H moves faster, while at acid *p*H, again unlike all the other known variants, it moves more slowly than haemoglobin A. In reticulocyte and sickling preparations of blood from the subjects with haemoglobin H intra-erythrocytic inclusion bodies were observed in nearly all the cells; these appeared to represent denatured haemoglobin H which, like haemoglobin S and unlike other variants, becomes much less soluble in the reduced state. Unlike all other known haemoglobins, haemoglobin H is rapidly denatured on storage, practically complete denaturation occurring as a result of a single freezing and thawing.

Neither of the parents of the subjects with haemoglobin H possessed the variant, but in the father and 2 of the subjects themselves the blood picture showed certain features consistent with possession of the thalassaemia trait, and the authors suggest that the most likely of several possible explanations is that a thalassaemia gene was inherited from the father and a gene for haemoglobin H, which shows penetrance only in the presence of the thalassaemia gene, from the mother.

H. Lehmann

397. **The Anemia of Infection. XX. The Kinetics of Iron Metabolism in the Anemia Associated with Chronic Infection**

J. A. BUSH, H. ASHENBRUCKER, G. E. CARTWRIGHT, and M. M. WINTROBE. *Journal of Clinical Investigation* [*J. clin. Invest.*] 35, 89–97, Jan., 1956. 3 figs., 36 refs.

The haematological and clinical aspects of the anaemia associated with chronic infection have been extensively studied, but its pathogenesis still remains obscure. A survey of the literature suggests that the profound alteration in iron metabolism may indicate a reduction in the life-span or rate of production of the erythrocytes. Using the method devised by Huff *et al.* (*J. clin. Invest.*, 1950, **29**, 1041; *Abstracts of World Medicine*, 1951, **9**, 63) for determining the turnover rate of radioactive iron (^{59}Fe) in plasma and erythrocytes, from which the life-span of the latter can be determined, the present authors, working at the University of Utah College of Medicine, Salt Lake City, have compared the findings in 6 patients with chronic infection (in 4 cases due to tuberculosis of different types) with those in 10 normal subjects.

The results showed that at first the incorporation of ^{59}Fe into the erythrocytes of the patients was initially more rapid than in the controls, but eventually between the 8th and 10th days the proportion of the isotope incorporated was the same in both groups (95%). The average "apparent" life-span of the erythrocytes was significantly shorter in the patients than in the controls; but this decrease in life-span was relatively small and could be met, the authors estimate, by a 50% increase in marrow activity. Discussing this point they state that normal bone marrow is capable of increasing its output of erythrocytes by 6 to 8 times, but in the patients with chronic infection not even an increase by one-half occurred, so that the patients became anaemic. It is therefore apparent, as other workers have noted, that there is a marked inhibition of erythropoiesis in patients with chronic infections.

M. C. G. Israëls

398 (*a*). **Mechanisms Involved in the Development of Vitamin B_{12} Deficiency**

J. A. HALSTED, M. E. SWENDSEID, P. M. LEWIS, and M. GASSTER. *Gastroenterology* [*Gastroenterology*] **30**, 21–36, Jan., 1956. 3 figs., 24 refs.

398 (*b*). **Intestinal Absorption and Hepatic Uptake of Vitamin B_{12} in Diseases of the Gastrointestinal Tract**

G. B. J. GLASS. *Gastroenterology* [*Gastroenterology*] **30**, 37–52, Jan., 1956. 8 figs., bibliography.

Of the investigations into the mechanisms of absorption of vitamin B_{12} (cyanocobalamin) from the gastrointestinal tract reported in these two papers, that of Halsted *et al.*, carried out at the Veterans Administration Center and the University of California, Los Angeles, was based on the familiar method of study by measuring the percentage excretion of an oral dose of cyanocobalamin labelled with radioactive cobalt (^{60}Co), whereas Glass, working at Flower and Fifth Avenue Hospitals (New York Medical College), New York, used a simpler but less well tried method based on the measurement with a scintillation counter of the concentration of ^{60}Co in the liver after an oral dose of labelled cyanocobalamin. The conclusions drawn from both are essentially the same.

Impairment of absorption of cyanocobalamin from the gastro-intestinal tract may be due to one of three mechanisms: (1) deficiency of gastric intrinsic factor; (2) interference by bacterial action in the small intestine ("blind-loop syndrome")—intrinsic factor is present in these cases, and the administration of aureomycin is the only proved method of reducing the faecal excretion of the vitamin; or (3) defective absorptive capacity of the intestinal mucosa, as in the sprue syndrome, when faecal excretion is unaffected by antibiotics or the addition of intrinsic factor. Glass, in studying 10 patients in this last group, found that in one case the administration of

corticotrophin materially enhanced the absorption of cyanocobalamin from the intestine. Cyanocobalamin deficiency rarely results from an inadequate intake in the diet, as the physiological requirements of the body are probably less than 1 μg. a day, but 2 probable cases of this type are reported by Halsted. In both papers the fact is stressed that optimum percentage absorption occurs with the smallest practicable test dose (0·5 μg.) and that any increase in this dose causes a rapid falling-off in the proportion absorbed. It is also pointed out that the body's reserves of cyanocobalamin are adequate to last 2 or 3 years in the absence of significant absorption.

In both investigations the absorption of cyanocobalamin in cases of megaloblastic anaemia following total and partial gastrectomy was found to be identical with that in pernicious anaemia. In addition, Glass found an impairment of absorption of cyanocobalamin, apparently due to partial failure of production of intrinsic factor, in elderly patients with gastric anacidity or hypoacidity and in some younger patients with anacidity. *John Naish*

399. **Treatment of Hypochromic Anemia with an Intramuscular Iron–Dextran Complex**
A. GRUNBERG and J. L. BLAIR. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **96**, 731–733, Dec., 1955.

Intramuscular injections of an iron–dextran compound were given to 30 patients with hypochromic anaemia at St. Catherine's Hospital, Birkenhead. There was rapid improvement in the haemoglobin level in all cases. The method used for estimating the amount of iron required by each patient is described; the authors state that this amount was increased by 50 to 80% to allow for replenishment of iron stores. Usually the patients received injections of up to 250 mg. on alternate days, but in 2 cases daily injections were given without any harmful effects. Local reactions were limited to slight discomfort and to staining at the injection site; no general reactions were observed.

[No reference is made to previous reports on intramuscular iron therapy which have already appeared in British journals: see *Abstracts of World Medicine*, 1955, **17**, 212, 258, 285, and 469.] *R. F. Jennison*

400. **Paroxysmal Nocturnal Hemoglobinuria: Report of Four Cases, with Observations on Treatment with 3:3′-Methylene-bis-(4-hydroxycoumarin) (Dicumarol)**
H. A. PERKINS, J. M. BOULWARE, T. V. FEICHTMEIR, W. W. THAYER, and T. H. SPAET. *Annals of Internal Medicine* [*Ann. intern. Med.*] **43**, 1218–1229, Dec., 1955. 1 fig., 11 refs.

The haemolysis of erythrocytes in paroxysmal nocturnal haemoglobinuria (P.N.H.) is accelerated by the presence of thrombin. This is the basis of Crosby's test (*Blood*, 1950, **5**, 843; *Abstracts of World Medicine*, 1951, **9**, 291), in which dicoumarol is used to decrease the formation of thrombin and thus to permit longer survival of P.N.H. erythrocytes. Since there are marked fluctuations in the severity of P.N.H., experience in a large number of cases is necessary before final conclusions can be drawn concerning the value of dicoumarol in the treatment of this disease.

In this paper from Stanford University School of Medicine, San Francisco, 4 new cases of P.N.H. are described and the differential diagnosis is discussed. Dicoumarol was given in each case, and although it seemed to decrease the rate of haemolysis, it did not control the disease completely. The authors state that there is evidence that the prothrombin concentration by Quick's method must be kept below 30% for effective control; even temporary loss of control may result in massive destruction of erythrocytes. They conclude that dicoumarol is indicated only in those cases of P.N.H. in which the rate of haemolysis is so rapid, or there are so many crises, that frequent admission to hospital and blood transfusions are necessary. Once dicoumarol therapy is started it should be continued for a prolonged period. *A. W. H. Foxell*

401. **Acute Vascular (Schönlein–Henoch) Purpura—an Immunologic Disease?**
M. B. KREIDBERG, W. DAMESHEK, and R. LATORRACA. *New England Journal of Medicine* [*New Engl. J. Med.*] **253**, 1014–1018, Dec. 8, 1955. 2 figs., 18 refs.

The authors describe 15 cases of Schönlein–Henoch purpura seen at the Boston Floating Hospital between 1948 and 1951 in patients aged 2 to 9 years, of whom 9 were girls and 6 boys. In 2 cases there was a personal history of allergy (asthma and sulphonamide sensitivity in one case and penicillin sensitivity in the other), and 3 had a family history of allergy. All the children were acutely ill. The usual clinical picture of purpura, sometimes with preceding urticaria, arthralgia with or without joint swelling, and intestinal colic often accompanied by melaena was seen. In all cases the history revealed an antecedent tonsillar or pharyngeal infection within the previous 4 weeks; 3 of the patients developed acute nephritis.

There was a mild to moderate anaemia, a normal or increased leucocyte count, with an eosinophilia in 5 of the cases, and a normal or slightly raised platelet count. Marrow biopsy in 4 cases revealed many megakaryocytes and masses of platelets. The blood clotting time was normal and blood cultures were negative. Skin biopsy examination (performed in 4 cases) revealed an acute inflammatory reaction centred round the capillaries, chiefly in the superficial corium, but affecting the more deeply situated arterioles also in the severer cases. This resulted in oedema in and around the vessel walls, extravasation of erythrocytes, and perivascular cuffs of polymorphonuclear leucocytes, lymphocytes, eosinophils, and histiocytes. There were no changes suggestive of a collagen disorder. Three of the patients who did not respond appreciably to conservative treatment lost their purpuric lesions within a week of a 14-day course of ACTH, one of these cases relapsing a week after cessation of therapy but thereafter regressing spontaneously.

The authors deduce the fundamental lesion to be a vasculitis and perivasculitis, the resulting haemorrhage and oedema producing the characteristic symptoms and signs. They suggest that the lesion may be an antigen-

antibody reaction at the vascular level arising, after a latent (incubation) period, as a result of a preceding infection. They believe this suggestion is supported by the facts that β-haemolytic streptococci were isolated from the throat of one of their patients, that other workers have produced a similar picture using hetero-immune anti-blood-vessel sera, and that the histological picture resembles that of periarteritis nodosa [in which, however, it is the larger blood vessels which are affected].

M. Kendal

402. Immediate and Remote Results of Chloroethylamine Treatment of Hodgkin's Disease

L. F. LARIONOV. *British Medical Journal* [*Brit. med. J.*] 1, 252–256, Feb. 4, 1956. 4 figs., 9 refs.

A report is presented on the use of 2-chloropropyl-di-(2-chloroethyl)-amine hydrochloride (" novoembichin ") in the treatment of some 300 cases of Hodgkin's disease at various institutions in Moscow and Leningrad. It is said to have milder side-effects on the gastro-intestinal tract and on the bone marrow than the other chloroethylamines which have been used. Doses of 8 to 10 mg. are given intravenously, usually thrice weekly, for 8 to 16 doses until the leucocyte count has fallen to 2,500 or 3,000 per c.mm.; if necessary, the treatment is continued further. The drug is of value both in the advanced stages of the disease and also in the early stages, in which life expectation and working capacity may be increased by more than 5 years in 50% of cases. The results are as good as, or better than, those obtained with radiotherapy. Combined methods of treatment have also been used, in which radiotherapy is applied to the lymph nodes.

Another member of the chloroethylamine group, 2:6-dioxy-4-methyl-5-(2-chloroethyl)-aminopyrimidine (" dopan "), has recently been investigated, and can be given orally with only slight toxic effects on the gastro-intestinal tract, 8 to 10 mg. being given twice weekly for about 3 to 5 weeks. Preliminary results suggest that it is as effective as novoembichin in Hodgkin's disease.

John F. Wilkinson

403. Fresh Blood Transfusion in Leukaemia

G. WETHERLEY-MEIN and D. G. COTTOM. *British Journal of Haematology* [*Brit. J. Haemat.*] **2**, 25–31, Jan., 1956. 14 refs.

The authors state that " certain features of the natural history of leukaemia suggest that the process may be partially or completely controlled by a humoral mechanism ", and quote the literature reporting remissions of leukaemia after blood transfusion, but are careful to point out that this experience has not been universal.

They then describe the effects on the leukaemic process of 77 blood transfusions given at St. Thomas's Hospital, London, to 23 patients with various types of leukaemia; the results are presented in tables. No complete or even partial remission followed the administration of fresh or stored blood. It was noted, however, that in cases of chronic myeloid leukaemia and lymphatic leukaemia 23 out of 26 transfusions of fresh blood produced a fall in the leucocyte count, whereas 13 transfusions of stored blood given to the same patients produced a fall in only 2 instances. In another group of 9 patients with acute or chronic myeloid leukaemia who were given 20 transfusions of fresh blood only, 15 of these caused a fall in the leucocyte count, 4 a rise, and one no change, whereas in 9 patients given stored blood only 5 out of 18 transfusions produced a fall in the leucocyte count. There was no change in the differential leucocyte count, but simply a decrease in the total count.

The authors suggest three possible explanations: (1) the fall may be caused by the non-specific stress caused by fresh blood transfusion; (2) fresh blood may contain a labile antileukaemic factor; or (3) fresh blood may contain a physiological leucocyte-controlling factor with no specific significance in leukaemia. They conclude by pointing out that the pattern of the leucocyte change in this series corresponds to the early phase of the transfusion-induced remission of leukaemia described by Dreyfus, and consider it probable that the mechanism in both cases is the same.

F. Hillman

404. Platelets in Stored Blood

J. F. MUSTARD. *British Journal of Haematology* [*Brit. J. Haemat.*] **2**, 17–24, Jan., 1956. 8 figs., 22 refs.

In view of conflicting reports regarding the preservation of platelets *in vitro* the author, working at the University of Cambridge, carried out a platelet count on 10 fresh samples of donor blood with " sequestrene " as anticoagulant, and on 10 samples of blood stored at 4° C. with A.C.D. (acid–citrate–dextrose) solution; the technique is described. The morphology of the platelets was studied under the phase-contrast microscope, and most of the tests were performed in duplicate.

The degree of platelet preservation in the 10 bottles after 21 days' storage ranged from 16 to 41% of the initial counts. The bottles showing the greatest loss of platelets during collection of the blood also showed the greatest loss during the early part of storage. Platelet function, as assessed by the thromboplastin-generation test, after 3 weeks' storage was 56 to 170% of the initial value. Phase-contrast microscopy showed fragmentation of the platelets and other changes characteristic of ageing. About 50% of the young platelets appeared to have dendrites, but with increasing age of the blood the dendritic forms were gradually replaced by smooth round forms, while later still ballooned forms with eccentric granules appeared. The calcium clotting time, prothrombin consumption, and thromboplastin generation, as measures of the thromboplastic activity of the blood under investigation, showed no loss of activity over the 21 days. During storage the thromboplastin activity of alumina-absorbed plasma and the one-stage prothrombin index did decline, the decrease being correlated with the loss in platelets.

In discussion the author states that the discrepancy between the figures here presented and those reported from North America may be related to the method of collection of the blood, namely, into vacuum bottles in North America and by gravity in Great Britain; the latter method gives " better numerical platelet preservation ".

F. Hillman

Respiratory System

405. **Reassessment of Value of Oxygen Masks that Permit Rebreathing**
J. E. COTES. *British Medical Journal* [*Brit. med. J.*] 1, 269–271, Feb. 4, 1956. 3 figs., 25 refs.

Recognition of the fact that carbon dioxide retention, which is dangerous to a dyspnoeic patient, may be accentuated by rebreathing during oxygen therapy has prompted the author to investigate, at the Pneumoconiosis Research Unit, Llandough Hospital, Penarth, Glamorganshire, the effects on ventilation of the Haldane and B.L.B. (Boothby, Lovelace, and Bulbulian) oxygen masks in healthy and in dyspnoeic individuals, with and without rebreathing. The results showed that rebreathing increases the ventilation by 52% but without additional benefit to the patient, who is often more uncomfortable. The Haldane and B.L.B. masks were devised for use on healthy people, and it is suggested that the patient with chronic chest disease will get most benefit from the administration of oxygen if the gas is inhaled from a mask furnished with a reservoir bag which is fitted with a valve to prevent rebreathing, as in the Haldane type, and that masks employing the rebreathing principle should not be used by such patients.

J. Robertson Sinton

406. **Reversal of Pulmonary Hypertrophic Osteoarthropathy by Vagotomy**
G. FLAVELL. *Lancet* [*Lancet*] 1, 260–262, Feb. 11, 1956. 6 refs.

Hypertrophic osteoarthropathy is found most typically as a secondary manifestation of a chronic pulmonary or cardiac disorder. It is extremely rare in chronic pulmonary tuberculosis, yet its association with bronchial carcinoma is well recognized. Indeed, a patient may be treated for as long as 12 months for "rheumatism" or "arthritis" before a neoplasm is revealed by radiography. In the experience of the present author joint pain occurs in 5 to 10% of cases of bronchial carcinoma, and careful inquiry usually shows that it was the first symptom to be noted.

It has long been known that resection of the growth is followed instantly by the cessation of all joint pain and the resolution of secondary changes in the nails, but no satisfactory explanation of the mechanism involved has been put forward. The author, in the belief that only the interruption of a neural reflex originating in the affected lung could explain the abrupt and consistent cessation of pain, has observed the effect on hypertrophic osteoarthropathy in a number of patients with inoperable bronchial carcinoma of (1) performing as complete a hilar clearance as possible on the affected side, dividing the pleural investment and all fibres of the vagus and sympathetic nerves entering the root of the lung; and (2) isolating and dividing the vagus branches to the affected lung, avoiding all interference with the rest of the hilum. Reports of 5 cases are given, 2 treated by the first and 3 by the second method. The effect was equally dramatic in all cases, with immediate and complete relief of joint symptoms, and resolution of joint effusions within a few days. Exploratory thoracotomy alone in 2 patients with clubbing and arthralgia had no effect.

D. P. McDonald

407. **The Haematological Manifestations of Primary Bronchopulmonary Carcinoma.** (Les manifestations hématologiques des cancers broncho-pulmonaires primitifs)
M. BARIÉTY and M. BOIRON. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] 32, 883–891, March 14, 1956. 6 figs. 30 refs.

The authors have studied the blood picture in 100 patients (97 men and 3 women) with primary bronchopulmonary carcinoma, cell counts being made in all cases and the results statistically analysed. Moderate anaemia was present in 72% of the cases and a more severe anaemia in 14%, the anaemia being of the normochromic or hypochromic type with the occasional presence of a normoblast. The total leucocyte count showed a consistent and significant increase in nearly every case, rising to more than 20,000 per c.mm. in 70% of the cases, the increase being mainly in the neutrophil granulocytes. An association was apparent between the neutrophilia, the type of pulmonary lesion, and the increased leucocyte count, the neutrophilia being particularly associated with epidermoid carcinomata and especially those complicated by atelectasis or tumour necrosis. The authors discuss the possibility of differentiating between a leucocytosis due to secondary changes in the lung and that due to the primary tumour, but come to no conclusion. There was also a consistent though slight increase in the eosinophil count, but this did not appear to be correlated with the clinical state. The lymphocyte count was almost always reduced whereas the monocyte count usually showed a significant increase.

The bone marrow was studied in 15 cases, all of which showed a hyperplasia, especially of the erythrocyte series; in 3 cases (20%) there were tumour deposits in the marrow, all 3 of the small-cell type. The authors suggest that the finding of lymphocytosis and erythroblastosis should always be an indication for sternal puncture, notably in suspected cases of anaplastic tumour, in which the formation of metastases is more common. Determination of the erythrocyte sedimentation rate in 55 of the cases showed it to be elevated in almost every case, even in the absence of infection, only 6 (10·9%) of the readings being within the normal range. Electrophoretic studies of the blood revealed that there was a considerable increase in the fibrinogen level and also some increase in those of α_2 and β globulins. They

emphasize that although these blood changes are non-specific in character, they may be a valuable aid to diagnosis.

[These blood changes in carcinoma have of course been known for some time, but the present authors have analysed them statistically and also discuss the pathogenesis very fully.] *R. F. Jennison*

408. **Chronic Pulmonary Disease as a Possible Etiologic Factor in Lung Cancer**

W. FINKE. *International Record of Medicine* [*Int. Rec. Med.*] **169**, 61–72, Feb., 1956. Bibliography.

The author reviews previous work on the relationship between pulmonary and bronchial infection and the development of bronchial cancer and presents new data on the frequency of previous respiratory disease in patients with bronchial cancer. The case records, and particularly the records of previous admissions, of 159 patients with bronchial cancer in three hospitals in New York State were examined; in the case of 76 patients treated at one hospital additional information was sought from the patients themselves, their relatives, and other persons or institutions who might have pertinent information. Full information extending back to childhood was obtained in this way in 50 cases.

Chronic cough was reported by 41% of the whole group of patients, by 40% of the sub-group of 76 patients, and by 75% of the special group of 50. The proportions giving a history of influenza or pneumonia in 1918–20 were respectively 17%, 8%, and 46%, and the proportions with a history of some chronic pulmonary disease (bronchitis, bronchiectasis, tuberculosis, or silicosis) were 34%, 28%, and 70%. The special group of 50 patients was also compared with 50 other patients of the same sex distribution admitted to the same hospital and with 136 working men and women and 271 ambulatory patients with other respiratory diseases. The results showed a higher proportion of heavy cigarette smokers and a higher incidence of influenza in 1918–20 and of non-influenzal pneumonia among patients with cancer than among the other in-patients. The incidence of influenza and pneumonia in the working population closely resembled that in the control group of in-patients, but the ambulatory patients with other respiratory diseases resembled the group with cancer in this respect. In the author's opinion " the results of this study support the view that chronic pulmonary disease may be one of the 'nearer causes' of bronchogenic carcinoma ".

Richard Doll

409. **Spiramycin in 18 Cases of Pulmonary Pneumococcal Infection in Africans.** (La spiramycine dans 18 cas de pneumococcies pulmonaires de l'Africain)

J. SOULAGE, G. CHARMOT, and J. DELAHOUSSE. *Presse médicale* [*Presse méd.*] **64**, 103–105, Jan. 21, 1956. 6 figs., 13 refs.

The authors report the results of the treatment with spiramycin of 18 African negro soldiers admitted to the Michel-Lévy Military Hospital, Marseilles, with acute pulmonary pneumococcal infections. In 2 cases there was a concomitant purulent pleural effusion, in 3 others evidence of hepatitis, and one patient had a complicating nephritis. The daily dosage of spiramycin ranged from 1·5 to 3 g. for 4 to 10 days, to a total of 5 to 26 g., except in the case of the patient with nephritis, who received 40 g. over a period of 15 days, and one other patient who probably had a pulmonary abscess and who was given 34 g. over 14 days. The results are described as " brilliant ". Pyrexia usually subsided within 24 to 48 hours, except in the patient with abscess of the lung in whom temperature was not normal until the 6th day. There were no signs of digestive intolerance or of avitaminosis. *I. Ansell*

410. **Use of Nitrogen Mustard in Treatment of Serous Effusions of Neoplastic Origin**

A. S. WEISBERGER, B. LEVINE, and J. P. STORAASLI. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 1704–1707, Dec. 31, 1955. 3 figs., 9 refs.

During a 2-year period at University Hospital, Cleveland, Ohio, 43 cases of serous effusion (30 pleural, 11 peritoneal, and 2 pericardial) of proved malignant origin were treated with nitrogen mustard, which has been shown to be effective in decreasing or eliminating re-accumulation of fluid. Approximately one-half of the effusion was removed by paracentesis, and the nitrogen mustard was instilled into the remainder. To ensure mixing the patient was moved several times. Good results were obtained in 28 cases (65%)—a figure which compares favourably with that achieved by radioactive gold treatment. Side-effects were much less than after the intravenous administration of nitrogen mustard. It is reported that 20 of the 28 patients are still living, with improvement lasting from 2 to 24 months.

G. Calcutt

411. **Parietal Pleurectomy for Recurrent Spontaneous Pneumothorax**

E. A. GAENSLER. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **102**, 293–308, March, 1956. 5 figs., 14 refs.

Writing from Boston City Hospital, the author stresses the frequency of spontaneous pneumothorax in apparently healthy young men, its liability to recurrence, and the added risk when it is bilateral. He reviews the various methods which have been tried for the treatment of the condition, states that conservative methods are unreliable [a view which is not widely held in Britain], and advocates surgical treatment for any patient in whom there has been more than one incident of leakage of air into the pleura. If obvious blebs or bullae are present these should be excised, but thoracoscopy should be undertaken before the exact type of operation is decided upon. In cases in which the disease process in the lung is found to be too extensive for resection, the author recommends excision of the parietal pleura over the affected part of the lung, removing if necessary the whole layer, with the exception of that over the diaphragm and mediastinum. He states that so far 9 of his patients have been treated in this way without complication, and none has shown any loss of pulmonary function.

J. R. Belcher

Otorhinolaryngology

412. **Treatment of Stammering Based on the Physiological Interpretation of its Mechanism.** (О лечении невроза заикания на основе физиологической трактовки его механизмов)
E. Z. Neĭmark. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **55**, 518–519, 1955.

Working at the neurological clinic of the State Balneological Institute, Sochi, the author describes a method of treating stammering involving the use of graduated noise transmitted through earphones worn by the patient, the treatment being given to groups of stammerers each of whom in turn was required to read aloud 20 to 30 minutes to the others in daily sessions. The noise in the earphones was loud enough at first to drown the sound to himself of the reader's own voice, and its intensity was then gradually reduced. It is stated that the method proved valuable in older patients, but it is not recommended in the case of young children as a substitute for normal speech training. *L. Crome*

[The employment of a very similar method of treatment with complete success in 24 out of 25 cases of stammering has recently been reported by Cherry *et al.* (*Nature* (*Lond.*), 1955, **176**, 874; *Abstracts of World Medicine*, 1956, **20**, 42).—Editor.]

413. **The Reaction of the Cochlea following a Fenestration Operation**
J. Venker. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **63**, 21–24, Jan., 1956. 13 refs.

During the 5-year period 1947–52 the author performed 402 fenestration operations for otosclerosis with a result that satisfied the patient in 76·4% of cases. He points out that an unsuccessful operation not only has a bad psychological effect on the patient, but also may change a conduction deafness into a nerve deafness which cannot be improved by a hearing aid. The cause of failure in 81 of his 96 unsuccessful cases was postoperative labyrinthine reaction, which he therefore regards as the most important of such causes. The author deliberately avoids using the term "labyrinthitis", which implies inflammation, in describing this reaction since little is known of its true nature. Fenestration is usually followed by immediate improvement, lasting for a few hours or days, after which perception diminishes, especially for tones above 1,000 c.p.s., hearing finally being restored after 7 to 14 days in favourable cases. The deeper the fall in acuity of hearing and the longer the period of depression, the poorer will be the end-result. During this period the ear shows recruitment, which was absent before operation. This must be due to a change in the hair-cells caused by opening the labyrinth, and as the only communication between the cochlea and the operative field is through the perilymph surrounding the membranous labyrinth, this fluid must presumably have become toxic to the hair-cells, probably, in the author's opinion, as a result of a change in its chemical composition.

The most recent estimates show that the perilymph and the cerebrospinal fluid (C.S.F.) have a similar crystalloid content, but that the total nitrogen content of perilymph is double that of the C.S.F. The sodium content of the endolymph is only one-tenth of that of the perilymph and C.S.F., but its potassium content is 20 to 30 times higher. This high potassium concentration is not found in any other free fluid of the body, and resembles that of the intracellular fluid.

It is usual to irrigate the operation field with isotonic saline throughout the fenestration operation. The author points out that this must alter the composition of the perilymph and—if the membranous labyrinth is permeable to crystalloids, as is widely held to be the case—of the endolymph too. To reduce this risk the author now uses an irrigation fluid approximating in osmotic pressure and composition to perilymph—Ringer–Locke solution with the addition of sodium chloride and serum albumin. Since adopting this measure in 1952 he has performed 77 fenestrations with only 6 failures, none of which was due to postoperative labyrinthine reaction. Moreover, the average functional gain in this series was 9·3 db. higher on the tenth postoperative day than in the earlier series. *F. W. Watkyn-Thomas*

414. **Arthritis of the Cricoarytenoid Joint**
W. W. Montgomery, P. M. Perone, and L. A. Schall. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol. (St Louis)*] **64**, 1025–1033, Dec., 1955. 16 refs.

Writing from the Massachusetts Eye and Ear Infirmary, Boston, the authors state that the causes of arthritis of the crico-arytenoid joint are: (1) direct extension of infection from the larynx or pharynx; (2) a general arthritis, especially rheumatoid arthritis; (3) trauma sustained during endoscopy; and (4) immobilization as a result of long-standing paralysis of the intrinsic laryngeal muscles.

In the acute stage the symptoms are hoarseness and pain. If both joints are involved there may be stridor and dyspnoea. Laryngoscopic examination shows marked redness over the arytenoid. The joint is found to be fixed when attempts are made to move it with a probe. The differential diagnosis from vocal-cord paralysis may be made on the history and on the result of trying to move the vocal cord with a probe. In the late stage of paralysis, however, the vocal cord will not move because of ankylosis of the crico-arytenoid joint. If both vocal cords are paralysed, there is no bowing of the cords in inspiration, such as can be seen in arthritis of the crico-arytenoid joint. The acute stage may require the performance of a tracheotomy. In the chronic stage the treatment is tracheotomy or removal of the arytenoid cartilage. *William McKenzie*

Urogenital System

415. **Comparison of Urography with Selective Clearance as Tests of Renal Function.** [In English]
N. P. G. EDLING, C. A. EDVALL, C. G. HELANDER, and B. PERNOW. *Acta radiologica* [*Acta radiol. (Stockh.)*] 45, 85–95, Feb., 1956. 7 figs., 8 refs.

In 23 patients with various renal lesions and impaired function who were studied at Karolinska Sjukhuset, Stockholm, the inulin clearance (glomerular filtration rate) and PAH clearance (renal plasma flow) were determined and the degree of impairment indicated by the results compared with that indicated by the density of the renal and pelvic shadows during excretion urography. Although there was generally a qualitative agreement between the results of the two types of test, there were a number of discrepancies, and the clearance results alone were of value as a quantitative measure of renal function. *D. A. K. Black*

416. **Amino-aciduria in Acute Tubular Necrosis**
D. EMSLIE-SMITH, J. H. JOHNSTONE, M. B. THOMSON, and K. G. LOWE. *Clinical Science* [*Clin. Sci.*] **15**, 171–176, 1956. 11 refs.

417. **Distal Tubular Necrosis with Little or No Oliguria**
S. SEVITT. *Journal of Clinical Pathology* [*J. clin. Path.*] 9, 12–30, Feb., 1956. 15 figs., 19 refs.

In this paper from the Birmingham Accident Hospital the author analyses the clinical and pathological features of the renal disturbance in 20 fatally burned subjects who were still able to excrete more than 300 ml. of urine a day despite the presence of severe kidney lesions. These were selected from a series of 86 patients with fatal burns, of whom 35 showed post-mortem evidence of distal tubular necrosis (synonymous with Lucké's "lower nephron nephrosis"), though only 12 developed severe oliguria or anuria (the urinary output being unknown in 3 cases). To the 20 are added one child with burns on whom no necropsy was performed and one case of post-traumatic uraemia.

The patients fell into two groups: those with and those without azotaemia. The former consisted of 6 burned adults or adolescents and one child together with the patient with post-traumatic uraemia. The mean area of burning was 58% of the body surface. There was haemoglobinuria in 5 cases, and pigmented urinary casts in all. The symptoms of incipient uraemia were often masked by those due to burning, and renal failure was usually not suspected until the end of the first week, when the blood urea level was found to be 280 to 360 mg. per 100 ml. The urea clearance was determined in 4 of these cases and was 13 to 18% of normal in 3 and 2·6% in one case. The urinary specific gravity was determined repeatedly in 2 cases and was fixed at 1010 to 1014. In 2 cases it was shown that the tubules retained considerable power to reabsorb sodium and chloride. At necropsy the kidneys in 5 of these 7 cases showed diffuse distal tubular necrosis. In one patient who survived only 2 days there were many haemoglobin casts in the collecting and distal secretory tubules and in the ascending and second convoluted tubules, while the tubular epithelium showed localized thinning and necrosis, particularly around casts. Many of the glomeruli were ischaemic and the proximal convoluted tubules showed mild degeneration. In the 4 patients who survived longer (6 to 16 days) the kidneys were swollen and the cortex wide. Histologically, there were haemoglobin and eosinophilic casts in the collecting tubules, discrete tubular necroses, tubular epithelial regeneration, lymphocytic infiltration especially around blocked and ruptured tubules and around veins, venous thrombosis in the boundary zone, and tubulo-venous anastomoses. Mild degenerative changes were often present in the proximal convoluted tubules, and there was glomerular ischaemia and medullary oedema. In the remaining 2 cases the renal findings were atypical, with evidence of acute degeneration of the proximal convoluted tubules superimposed on a distal tubular necrosis, still active in one and recently healed in the other.

The second group of patients, those without oliguria or azotaemia, did not differ significantly from the first in respect of the mean burned area (52%), but in contrast it included 13 children and only one adult, while in only 4 cases was there haemoglobinuria (probably significant in 2 only). The blood urea level in 8 cases was 26 to 61 mg. per 100 ml., the urea clearance was normal in all 6 cases in which it was determined, and in 2 cases the renal concentrating power was shown to be moderately good. Post mortem the kidneys in all but one of this group showed focal distal tubular necrosis. In 2 early cases (death within 16 hours of burning) there were congestion, a few haemoglobin casts, and early discrete necroses in blocked tubules. A later phase was seen in 3 cases (6, 8½, and 35 days after burning), in which there were casts in a few distal convoluted and straight Henle tubules and some tubular regeneration. Foci of lymphoid cells were seen around diseased tubules and boundary-zone veins, and there were occasional organizing venous thrombi. In 8 patients who died 2 or 3 weeks after burning the disease process was either healing or healed, there being persistent, although scanty, evidence of tubular necrosis and regeneration in some cases, while in others only lymphoid-cell foci and organizing thrombi remained. The single atypical case differed from the rest in that multiple haemoglobin casts were present in the collecting tubules and the ascending and convoluted parts of the distal tubules, together with a few isolated necrotic foci.

It would thus appear that the essential difference between diffuse and focal distal tubular necrosis is in the extent of the lesion, which also determines the presence

or absence of uraemia. It is evident that uraemia may occur after burns in the presence of a normal urinary volume, and that its development may be masked by other symptoms and hence go untreated.

[This is an important paper and should be studied in detail by all concerned with the management of the burned patient.] *M. C. Berenbaum*

418. **The Effect of Reserpine and its Combination with Hydralazine on Blood Pressure and Renal Hemodynamics during the Hypertensive Phase of Acute Nephritis in Children**

J. N. Etteldorf, J. D. Smith, and C. Johnson. *Journal of Pediatrics* [*J. Pediat.*] **48**, 129–139, Feb., 1956. 15 refs.

The effect of reserpine on 20 children between the ages of 3 and 10 years with acute nephritis and hypertension was studied. The duration of illness before admission to hospital varied from 3 to 12 days, except in one case in which it was 30 days. The blood pressure in all cases was 140/90 mm. Hg or more on admission, this hypertension persisting after 6 to 12 hours' bed rest and phenobarbitone therapy. There was no evidence of heart failure or encephalopathy.

Reserpine alone was given to 10 patients in doses of 0·07 mg. per kg. body weight intramuscularly. In 4 the blood pressure fell satisfactorily within 20 to 30 minutes and continued to fall for 3 hours, the patients remaining normotensive thereafter. The 6 patients who did not respond to reserpine alone then received hydrallazine intramuscularly in doses of 0·15 mg. per kg. The blood pressure began to fall within 20 to 30 minutes and continued to fall during the following 2 to 10 hours, remaining normal in 3 cases; the 3 remaining patients, although responding well initially, required 2 further doses of reserpine and hydrallazine, and in one case a further dose of reserpine, before they remained normotensive.

Reserpine and hydrallazine were given simultaneously to another 10 children, 7 of whom became and remained normotensive, while 3 required further doses, one of these receiving both drugs daily for 11 days. The average time taken for the effect of the drugs to be seen when given together was 50 minutes, and the average time for the maximum response was between 4 and 5 hours. No undesirable side-effects were noted. Renal function studies were performed on most of these patients while under treatment and showed minimal changes attributable to the drugs. *C. Bruce Perry*

419. **Evidence of the Presence of a Pitressin-like Substance in the Tissue Fluids in Nephrosis.** [In English]

H. E. C. Wilson and A. Muirhead. *Acta paediatrica* [*Acta paediat.* (*Uppsala*)] **45**, 77–84, Jan., 1956. 9 figs., 12 refs.

In this paper from the Royal Hospital for Sick Children, Yorkhill, Glasgow, the authors report their investigations into the properties of the pressor substance found in the urine, ascitic fluid, and plasma in nephrosis. They found its characteristics to be similar to those of pituitary vasopressin both on electrophoresis and on paper chromatography with phenol. It was also, like vasopressin, destroyed by incubation with thioglycollate. [They do not appear, however, to have controlled their investigations by searching for a similar pressor substance in normal body fluids.]

They suggest that in nephrosis there is an initial sodium retention and that the resultant increase in sodium concentration stimulates the production of antidiuretic hormone by the posterior pituitary. *G. A. Smart*

420. **Use of Malaria Therapy in the Nephrotic Syndrome**

A. S. Gilbertsen and F. Bashour. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 25–30, Jan. 7, 1956. 2 figs., 19 refs.

This is a report from the University of Minnesota Hospitals, Minneapolis, on 6 patients with the nephrotic syndrome who were treated by infection with malaria (*Plasmodium vivax*); all of them were thought to be in the nephrotic phase of glomerulonephritis. In only 5 of them did malaria develop after inoculation, but in 4 of these a diuresis occurred. Of 3 of the patients who had hypertension, 2 had a diuresis with residual proteinuria, while in the third there was also nitrogen retention and no response was obtained. However, both the other 2 patients had a marked diuresis, the proteinuria disappearing immediately after malaria therapy in one, and spontaneously 3 months later in the other.

One of the patients treated successfully had previously been treated unsuccessfully with cortisone, and one of those who had a diuresis with residual proteinuria had previously shown no response to cortisone. It would seem that hypertension is not a contraindication to malaria therapy, as it is to treatment with cortisone or ACTH. *G. A. Smart*

421. **Production of Renal Ischemia and Proteinuria in Man by the Adrenal Medullary Hormones**

S. E. King and D. S. Baldwin. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 217–224, Feb., 1956. 4 figs., 26 refs.

The occurrence of transient proteinuria has been demonstrated in normal subjects following psychogenic stimuli, exposure to cold, and erect immobilization in lordosis. The intense renal vasoconstriction which occurs in these circumstances and accounts for the proteinuria is often accompanied by vasomotor phenomena suggesting sympathetic excitation, such as sweating, pallor, and tachycardia. The possibility that the mechanism leading to renal ischaemia is mediated through the adrenal medullary hormones was explored by the authors at the U.S. Army Renal Research Laboratory by observing the effect of intravenous infusions of L-noradrenaline and of adrenaline on 6 normal subjects and on 6 persons with orthostatic proteinuria. The response of normal subjects and persons with orthostatic proteinuria to the infusion of L-noradrenaline was similar, proteinuria occurring in 4 out of 5 of the former and 4 out of 5 of the latter, while adrenaline infusions given to 2 of the normal persons and to 2 with orthostatic proteinuria resulted in proteinuria in all 4. Tests of renal haemodynamics showed that an over-all increase in renal vascular resistance occurred as a result of the infusion of either drug. *G. W. Csonka*

Endocrinology

422. **Relationship between Diurnal Variations in Urinary Volume and the Excretion of Antidiuretic Substance**
R. GOLDMAN and E. B. LUCHSINGER. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **16**, 28–34, Jan., 1956. 24 refs.

In an attempt to determine whether the normal diurnal variation in water excretion (high during the day and low at night) and its inversion in patients with congestive heart failure or with hepatic cirrhosis and ascites are attributable to variations in the secretion of pituitary antidiuretic hormone the hormone was extracted from human urine by adsorption on zinc ferricyanide and assayed by intraperitoneal injection into rats during water diuresis, a method giving quantitative recovery of added vasopressin. Measurable antidiuretic activity (4 to 171 milliunits per 8 hours) was detected by this method, but the quantities excreted in the urine were in most cases greater when the urine volume was high—that is, during the day in 9 normal subjects and during the night in 11 patients with congestive heart failure or cirrhosis.

There is no absolute proof that the activity measured was in fact due to the presence of antidiuretic hormone, and even if it was, its urinary excretion may not truly reflect its rate of endogenous secretion. However, these results certainly provide no support for the theory that the diurnal variation in urine output is regulated by variations in the secretion of antidiuretic hormone.

Peter C. Williams

423. **Diabetes Insipidus in Association with Post-partum Hypopituitarism**
T. DOXIADES and M. TILIAKOS. *British Medical Journal* [*Brit. med. J.*] **1**, 23–25, Jan. 7, 1956. 21 refs.

424. **Simmonds' Disease. Evaluation of Certain Laboratory Tests Used in Diagnosis**
P. P. VANARSDEL and R. H. WILLIAMS. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 4–14, Jan., 1956. 2 figs., bibliography.

This paper from the University of Washington School of Medicine, Seattle, is based on the records of 62 patients with thyroid hypofunction secondary to pituitary disease and of 33 patients with primary myxoedema. The results of the usual tests of endocrine function are reported and contrasted in the two groups, including radioactive iodine absorption studies and estimations of the serum cholesterol content, basal metabolic rate, serum protein-bound iodine content, urinary 17-ketosteroid excretion, and insulin tolerance. The paper is, however, principally concerned with the significance of estimations of the urinary excretion of gonadotrophin (F.S.H.), which was assayed by the methods of Heller and Heller (*J. clin. Invest.*, 1939, **18**, 171), that of Bradbury *et al.* (*Proc. Soc. exp. Biol. (N.Y.)*, 1949, **71**, 228), or that of Gorbman (*Endocrinology*, 1945, **37**, 177).

Except for 2 women, in none of 43 of the patients with hypopituitarism was any excretion of F.S.H. detectable, whereas all but 3 of 19 of the patients with primary myxoedema excreted some of the hormone, usually in relatively high concentration. It is therefore concluded that, in the invidual case, assay of F.S.H. excretion does not provide a reliable differentiation between hypopituitarism and primary myxoedema. The authors consider it likely that with improved methods of assay it will be possible to detect some F.S.H. in the urine of all postmenopausal women with primary myxoedema, and that in women of this age with hypothyroidism the absence of F.S.H. excretion is almost certainly diagnostic of hypopituitarism. The presence of F.S.H. in the urine does not, however, exclude hypopituitarism, which in some cases may be incomplete, with preservation of some degree of gonadotrophic function. In men and premenopausal women normal excretion of F.S.H. is to be expected if primary myxoedema is present, and in the few cases in which the secretion of F.S.H. is below normal it will be increased on the administration of thyroid.

The authors also report the response to exogenous thyrotrophin in 4 cases of primary myxoedema and 7 cases of hypopituitarism and analyse the findings of previous workers. They conclude that, with modern preparations of this hormone, a response is to be expected unless thyroid atrophy is present. However, atrophy may occur in long-standing hypopituitarism as well as in myxoedema.

H.-J. B. Galbraith

425. **Changes in the Electroencephalogram Associated with Hypopituitarism Due to Post-partum Necrosis**
R. R. HUGHES and V. K. SUMMERS. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **8**, 87–96, Feb., 1956. 14 figs., 10 refs.

At the Royal Southern and Walton Hospitals, Liverpool, electroencephalograms (EEGs) were recorded in 14 cases of hypopituitarism due to post-partum necrosis. Specimens of the EEG tracings and summaries of the biochemical and clinical findings are given for each case.

In 10 cases in which hypopituitarism was severe the EEG showed marked diminution or complete absence of the alpha rhythms, which were replaced by generalized theta rhythms at 4 to 6 c.p.s. On overbreathing this activity became more irregular. Delta rhythms, if present in the resting record, were increased by overbreathing. The EEG was not so markedly abnormal in the 4 milder cases. Alpha rhythm was seen in 3 cases, one of which showed considerable clinical improvement with hormone therapy. It is stated that " the changes in the EEG are the result of endocrine disturbance and are not the result of organic brain damage ".

William Cobb

THYROID GLAND

426. The Genesis of Thyroid Adenomas

H. ZONDEK and H. LESZYNSKY. *Lancet* [*Lancet*] **1**, 77–78, Jan. 14, 1956. 14 refs.

The authors, working at the Biccur Cholim Hospital (Hebrew University), Jerusalem, have studied the course of hypothyroid nodular goitre in 2 siblings, a youth aged 17 and his sister aged 12, who were suffering from familial sporadic cretinism. As a result of treatment with triiodothyronine in doses of 960 μg. and 820 μg. respectively the thyroid gland in both cases showed a general reduction in size and most of the nodules which were present before treatment could no longer be palpated; in each case, however, one nodule remained despite intensive thyroid therapy.

Both patients were then allowed to relapse in order to study the effect of the goitrogenic agent on the structure of the gland. In both cases clinical relapse was accompanied by rapid re-formation of the goitre, the diffuse enlargement seeming to precede the appearance of the nodules, which occupied the same sites as before treatment; their size, however, could not be correlated with the rate or intensity of either their regression or reappearance. Subsequent treatment with thyroid produced the same effect as had been noted previously; in both cases the single nodule resistant to treatment was removed and showed the characters of a colloid adenoma. Studies with radioactive iodine on the male patient showed that both nodular and diffuse areas of the thyroid gland showed a similar uptake, and that although one nodule collected three times as much iodine as the rest of the gland, it responded to therapy (and its subsequent withdrawal) in the same way as the less active nodules.

The authors conclude that local differences in responsiveness to the goitrogenic agent, presumably thyrotrophic hormone, were responsible for the behaviour of the nodules. What is not known is the nature of the inherent factors which determine this responsiveness.

D. G. Adamson

427. Struma Lymphomatosa: Primary Thyroid Failure with Compensatory Thyroid Enlargement

P. G. SKILLERN, G. CRILE, E. P. MCCULLAGH, J. B. HAZARD, L. A. LEWIS, and H. BROWN. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **16**, 35–54, Jan., 1956. 2 figs., 41 refs.

In this paper from the Cleveland Clinic Foundation, Cleveland, Ohio, the authors present evidence in support of the contention that struma lymphomatosa (Hashimoto's disease) is not a true thyroiditis but is due to primary failure of thyroid function with compensatory hyperplasia and secondary lymphocytic infiltration and fibrosis. Their observations were made on 36 patients (33 women and 3 men) ranging in age from 12 to 59 years in whom the diagnosis of struma lymphomatosa had been confirmed by needle biopsy. In all cases there was diffuse enlargement of the thyroid gland, which was of firm consistency, the duration of the goitre being less than 10 years. Clinical signs of thyroid failure were present in 10 cases, with frank myxoedema in 2, while laboratory investigations and the clinical response to thyroid extract suggested that a state of "compensated" thyroid failure existed in many others. The basal metabolic rate in 22 cases was −15% or below, and the serum cholesterol content was greater than 250 mg. per 100 ml. in 9 cases. The serum gamma-globulin level was increased and that of albumin decreased in 16 cases, a finding which is attributed to thyroxine deficiency. Estimations of the uptake of radioactive iodine gave inconclusive results in the 26 cases studied.

Needle biopsy of the thyroid gland in 30 cases showed hyperplasia, eosinophilic changes in the cytoplasm of the thyroid cells, and small follicles separated by an infiltrate of lymphocytes, with or without fibrosis. In 4 cases there was a similar hyperplasia of the thyroid cells, but eosinophilic change was slight or absent; there was lymphocytic infiltration between the follicles, but only mild fibrosis. In the remaining 2 cases the appearances were intermediate between those of the two types described above. In most cases treatment with desiccated thyroid resulted in a significant decrease in the size of the goitre, the dose inducing this decrease most consistently being 3 grains (0·2 g.) daily.

The authors suggest that in struma lymphomatosa the basic defect is a primary failure of the thyroid cells, resulting in a deficient output of thyroxine. This leads to increased production of pituitary thyrotrophic hormone, which causes hyperplasia of the thyroid tissue. Lymphocytic infiltration and fibrosis are regarded as probably secondary to the failure of the thyroid cells rather than its cause. The cause of the thyroid failure is unknown, but in a few cases in the present series the stress of pregnancy seemed to have played a part. It is suggested that since the goitre of struma lymphomatosa is probably due to compensatory enlargement of a failing gland, and since the diagnosis can be made by needle biopsy, there is little reason for surgical treatment, which is frequently followed by clinical thyroid failure and further hyperplasia of the residual thyroid tissue, so that treatment with desiccated thyroid is necessary in any event.

John Lister

428. The Effects of Thyrotropin and Desiccated Thyroid upon Hypothyroidism with Goiter

R. P. LEVY, L. W. KELLY, and W. M. JEFFERIES. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **231**, 61–68, Jan., 1956. 2 figs., 16 refs.

While enlargement of the thyroid gland accompanied by increased thyroid uptake of radioactive iodine (^{131}I) usually indicates the presence of hyperthyroidism, this combination of findings sometimes occurs in cases of hypothyroidism. Three types have been described: (1) that seen in goitrous cretins, usually living in iodine-deficient regions where goitre is endemic; (2) a type seen in certain hypothyroid children in non-endemic regions who are thought to suffer from a familial defect in the synthesis of thyroid hormone; (3) a type recently described, lymphocytic thyroiditis, associated with histological changes in the gland.

At the Western Reserve University Hospitals, Cleveland, Ohio, the response to thyrotrophin and thyroid

extract was studied in 7 cases of hypothryoidism with goitre and increased uptake of ^{131}I, the series comprising 6 children aged 2½ to 12½ and one woman aged 47. In the 4 previously untreated cases thyrotrophin had no effect on the uptake of ^{131}I. However, treatment with desiccated thyroid relieved the symptoms and resulted in a decrease in the size of the gland. The patients were considered to be suffering from defective synthesis of thyroid hormone, which was causing increased pituitary output of thyrotrophin and consequent goitre.

G. S. Crockett

429. **The Effect of 3:5:3′-Tribromo-DL-thyronine in Myxoedema**

N. COMPSTON and R. PITT-RIVERS. *Lancet* [*Lancet*] 1, 22–23, Jan. 7, 1956. 2 figs., 2 refs.

DL-Tribromothyronine, a non-iodine-containing analogue of thyroxine, was used in the treatment of 2 myxoedematous patients. The patients' metabolism was restored to normal with a dose of 1 mg. daily, which is therefore considered to be equivalent to the dose of 0·4 mg. of L-thyroxine which, in the form of desiccated thyroid, had the same clinical effect. Since the D-isomer is probably inert it is considered that tribromothyronine in its laevo form has only slightly less thyroid-like activity than thyroxine.

John F. Wilkinson

430. **Metabolic and Therapeutic Effects of Triiodothyronine**

T. F. FRAWLEY, J. C. MCCLINTOCK, R. T. BEEBE, and G. L. MARTHY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 646–652, Feb. 25, 1956. 4 figs., 18 refs.

A series of 13 patients (11 adults, 2 children aged 10 and 15 years respectively) with the classic clinical picture of myxoedema were selected for study at the Albany Hospital, Albany, New York, the diagnosis being confirmed by estimation of the serum protein-bound iodine (P.B.I.) content and of the 24-hour uptake of radioactive iodine. The myxoedema was primary in 7 of the adult cases, postoperative in 3, and due to struma lymphomatosa in one. Over a period of 2 years the effects of oral medication with DL-triiodothyronine (25 to 400 μg. daily), L-triiodothyronine (100 to 200 μg. daily), sodium L-thyroxine (100 to 500 μg. daily), and desiccated thyroid (average daily dose 86 mg.) on the metabolism were compared. [It is not clear whether every patient received all four drugs or, if so, in what order.]

The four substances appeared to give comparable and satisfactory relief from the clinical and metabolic manifestations of myxoedema. In one case, however, there was no response to thyroid in a maximum daily dose of 768 mg., but a satisfactory response to DL-triiodothyronine (50 to 200 μg. daily) and L-thyroxine (200 to 500 μg. daily). In a single case of malignant exophthalmos the effect of DL-triiodothyronine (50 to 200 μg. daily for 3 weeks) was disappointing.

In comparison with the older preparations triiodothyronine was more rapid in taking effect, clinical improvement and a rise in body temperature, basal metabolic rate, and pulse rate being obvious within 72 hours of starting treatment, but in contrast to thyroid and L-thyroxine triiodothyronine caused only a very slight rise in the serum P.B.I. level, even when the patient had attained the euthyroid state. The side-effects of triiodothyronine did not differ qualitatively or quantitatively from those usually associated with the effective treatment of severe myxoedema, but sudden and marked recurrence of the symptoms and manifestations of hypothyroidism occurred within 24 hours of withdrawal of the drug.

From the clinical and metabolic data in these cases the authors estimate that the effects of triiodothyronine persist for less than 3 days after cessation of treatment. Hence maintenance therapy with another preparation should be started several days before the withdrawal of triiodothyronine. Dose for dose, L-triiodothyronine appeared to be twice as effective as the racemic form and 1½ to 2½ times more effective than sodium L-thyroxine. This suggests that the activity of the racemic form is due entirely to its content of the laevo isomer. The absence of any increase in the serum P.B.I. level after the administration of the new compounds may be due to rapid removal of triiodothyronine from the extracellular to the intracellular compartment. Although the significance of triiodothyronine in thyroid physiology is not yet clearly defined, it seems likely that this substance is produced by enzymatic deiodination of thyroxine in the peripheral tissues.

Marcel Malden

431. **Alterations in Thyroid I-131 Uptake, Basal Metabolic Rate and Serum Cholesterol following Treatment of Hyperthyroidism with Radioactive Iodine**

A. L. SCHULTZ and L. ZIEVE. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 30–41, Jan., 1956. 2 figs., 10 refs.

Clinical improvement after treatment with radioactive iodine (^{131}I) for hyperthyroidism is gradual, the full effect being appreciated only after several months, when in some cases treatment may have to be repeated to secure euthyroidism. A method whereby the need for such further therapy could be assessed within a few weeks of giving the first dose would therefore be of great value. In an attempt to determine the value of various laboratory tests for such an assessment the authors investigated 66 patients with hyperthyroidism approximately 6 weeks after a therapeutic dose of ^{131}I had been given. These patients, who were treated at the Veterans Administration Hospital, Minneapolis, formed an unusual group in that all but 4 were men and all but 6 had a diffuse goitre.

Even as early as 6 to 9 weeks after treatment the uptake of ^{131}I by the thyroid gland provided a clear indication of the final clinical result in most cases, while the changes in the basal metabolic rate (B.M.R.) and, to a lesser extent, in the serum cholesterol level were suggestive of the eventual outcome, at least so far as failure of therapy was concerned. The most accurate indication was given by a combined assessment of the clinical features and the results of ^{131}I uptake, B.M.R., and serum cholesterol estimations by means of a numerical rating system.

From their results the authors conclude that when the patient is still clinically hyperthyroid 6 weeks after treat-

ment, if both the ^{131}I uptake and B.M.R. are abnormally high or on the borderline, he should be re-treated, but if either is normal the course is uncertain and further observation is advisable.

The 21 patients in the authors' series who failed to become euthyroid after a first dose of ^{131}I (giving approximately 100 μc. per g. of thyroid tissue) were among the most severely thyrotoxic patients initially, whereas the 14 who eventually, after one or more treatments, became hypothyroid were among the least thyrotoxic. *H.-J. B. Galbraith*

432. An Evaluation of the Use of Radioiodine in the Diagnosis of Hyperthyroidism

G. R. FRYERS. *British Journal of Radiology* [*Brit. J. Radiol.*] **29**, 24–31, Jan., 1956. 11 figs., 19 refs.

A critical comparative study of some 15 different diagnostic tests for hyperthyroidism based on the use of radioactive iodine (^{131}I), as proposed by various workers, has been made by the author at the United Leeds Hospitals between 1949 and 1954. A single dose of 25 to 30 μc. of carrier-free ^{131}I in water was given by mouth to the patients, and specimens of urine were then collected over the next 48 hours. The estimations of blood level and thyroid uptake of ^{131}I were carried out in the usual manner. In each of 111 cases the results of 14 different tests were compared with estimates of the thyroid state based on the results of clinical tests only. The author concludes that the initial thyroid uptake and the urinary excretion of ^{131}I appear to provide the most reliable information for use in the diagnosis of thyrotoxicosis. *G. B. West*

433. An Evaluation of Various Factors Influencing the Treatment of Metastatic Thyroid Carcinoma with I^{131}

F. MALOOF, A. L. VICKERY, and B. RAPP. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **16**, 1–27, Jan., 1956. 13 figs., 31 refs.

The usefulness of radioactive iodine (^{131}I) in the treatment of metastatic thyroid carcinoma is limited by the failure of the tumour in most cases to concentrate enough of the isotope to be of therapeutic value. Various measures have therefore been employed at the Massachusetts General Hospital (Harvard Medical School), Boston, in an attempt to increase the uptake of ^{131}I by metastatic thyroid carcinomata. In 15 out of 21 selected cases total thyroidectomy was performed in order to induce function in the metastases. As a result of this procedure an uptake of ^{131}I was induced in the metastases in 7 cases and the previous uptake increased in 5 others. A concomitant growth stimulus was, however, also imparted to the metastases. The administration of antithyroid drugs to 14 of the 21 patients also increased ^{131}I uptake of the metastases in 8 cases, but increased the rate of growth of the metastatic lesions in 9. Another factor limiting the value of ^{131}I treatment is that owing to variations in function and histological pattern one metastasis may retain and concentrate ^{131}I well, whereas others in the same patient may concentrate very little, while others again may concentrate the isotope yet rapidly discharge it. Their response to treatment is thus very variable. The only serious complications of ^{131}I therapy encountered were due to its effect on the haematopoietic system. A fall in the leucocyte count, particularly affecting the lymphocytes, occurred in all cases, but was transient except in one patient in whom the haemoglobin level also decreased and who eventually died with a peripheral pancytopenia. Another patient, who developed ecchymoses in the skin, had a decreased platelet count with a normal bone marrow.

The restricted usefulness of ^{131}I in the treatment of these cases led the authors to treat a few patients with desiccated thyroid or testosterone in an attempt to inhibit the growth of the metastases by depressing pituitary activity. It appeared that thyroid therapy was of some value in those cases in which the metastases were able to concentrate ^{131}I, but it had no obvious influence in one case in which no concentration of ^{131}I had occurred. No effect was seen on the function or growth of the metastatic lesions in patients given testosterone. *John Lister*

PANCREAS

434. Demonstration of Antibodies to Insulin in Diabetics with Insulin Resistance by Means of the Haem-agglutination and Coombs Tests. (Nachweis von Insulin-antikörpern bei Diabetikern mit Insulinresistenz im Hamägglutinationstest und Coombstest)

H. STEIGERWALD and W. SPIELMANN. *Klinische Wochenschrift* [*Klin. Wschr.*] **34**, 80–84, Jan. 15, 1956. 2 figs., 10 refs.

Antibodies against insulin were demonstrated in the blood of a number of patients with insulin resistance at the University Medical Clinic, Frankfurt am Main, by the following methods. Rhesus-negative erythrocytes, washed twice in saline, were suspended in a 1 : 40,000 solution of tannic acid (*p*H 7·2) for 30 minutes at 37° C.; they were then washed again twice in saline and suspended in a solution containing 1 mg. of crystallized insulin per ml. with phosphate buffer (*p*H 5·5 to 6·0) for 30 minutes at 37° C. and for one hour at 4° C. A 2% suspension of these erythrocytes in a neutral buffered saline solution was then prepared, and 0·05-ml. amounts of the suspension mixed with 0·2 ml. of serial dilutions of the serum to be tested, a minute drop of the well-shaken mixture from each tube being examined under the microscope for agglutination of the cells after 2 and again after 24 hours. To exclude possible errors due to the presence of incomplete antibodies a rabbit was injected with the serum of an insulin-resistant diabetic and this rabbit's serum used for Coombs tests by the usual technique. The tests proved much more sensitive (and accurate) than the agglutination tests. Controls with serum obtained from rabbits immunized against normal serum globulin or with a commercial anti-globulin preparation were applied extensively to avoid misleading observations.

The titre of insulin antibodies, when present, in the blood of an insulin-resistant individual is liable to vary

for no obvious reason, but increases during infective illnesses, this explaining the increased insulin requirements of the diabetic in such circumstances. On the other hand although insulin antibodies can be demonstrated more frequently than has previously been thought, they are absent in the majority of cases of insulin resistance. *L. H. Worth*

435. **The Course and Complications of Diabetes Mellitus. Data in 331 Cases Observed Regularly in a Diabetic Clinic**

E. P. RALLI, E. STREET, and S. PELL. *Diabetes* [*Diabetes*] 4, 456–464, Nov.–Dec., 1955. 7 refs.

The authors have reviewed all the patients (126 men and 205 women) attending diabetic clinics at Bellevue Hospital, New York, between November, 1950, and April, 1951. Of the 331 patients, 81% were over 50 years old, and 19% over 70. The peak incidence of onset was in the age group 50–59, and diabetes had been present for 15 or more years in 27%. Nearly one-third (98) did not require insulin to control the glycosuria. Study of the relationship between severity of the diabetes (as judged by the total daily dose of insulin), age at onset, and duration of the disease showed that cases with onset in early life needed higher dosage than those with later onset; but when the age at onset was held constant there was no correlation between the patient's age and the severity of the diabetes.

A special study was made of 194 of the patients who had attended the clinic for 5 or more years. From this it emerged that a family history of diabetes was associated with an earlier onset of the disease than the absence of such history, but was not associated with greater severity. No case of retinopathy having apparently developed before the onset of the diabetes was observed. In 8 (18%) of the 44 cases of retinopathy the diabetes was known to have been present for less than 6 years. Other complications such as hypertension, hyperthyroidism, and gall-bladder disease are also discussed, the relation between the incidence of these complications and age at onset and duration being presented in numerous tables. *T. D. Kellock*

436. **The Controlling Action of *para*-Aminobenzenesulphonamido*iso*propylthiodiazol in Experimental Diabetes Mellitus.** (Action curatrice du para-aminobenzènesulfamidoisopropyl-thiodiazol sur le diabète sucré expérimental)

A. LOUBATIÈRES, P. BOUYARD, and C. FRUTEAU DE LACLOS. *Diabète* [*Diabète*] 4, 38–40, Jan.–Feb., 1956. 4 figs., 7 refs.

The administration by various routes of *p*-aminobenzenesulphonamido*iso*propylthiodiazol (PASIT) has been shown to produce prolonged hypoglycaemia in normal animals of a number of species, including man. In investigations here reported from the University of Montpellier PASIT in suitable dosage administered daily to dogs resulted in a permanent hypoglycaemia, and there was histological evidence of damage to the α cells of the pancreas. The drug had no action on pancreatectomized animals. Administration of PASIT to alloxan-diabetic rabbits and dogs restored the blood sugar level to normal, eliminated the glycosuria, and checked the loss of weight. Alloxan diabetes appeared to be cured permanently by PASIT in rabbits and in dogs with a mild degree of diabetes (though severe diabetes in dogs was not entirely controlled). Further treatment with alloxan caused reappearance of glycosuria, which was again reduced by administration of PASIT. It is suggested that the toxic effect of alloxan on some of the β cells, which results in glycosuria, is offset by the similar action on the α cells of PASIT, which also stimulates the activity and regeneration of the β cells. The implications of these findings for the pathogenesis and treatment of diabetes mellitus are discussed briefly. *F. W. Chattaway*

437. **The Inhibition of Insulinase by Hypoglycemic Sulfonamides**

I. A. MIRSKY, G. PERISUTTI, and D. DIENGOTT. *Metabolism* [*Metabolism*] 5, 156–161, March, 1956. 3 figs., 14 refs.

In experiments carried out at the University of Pittsburgh the authors have investigated the mechanism by which certain sulphonamides cause hypoglycaemia. The sulphonamides studied were 1-butyl-3-*p*-aminobenzenesulphonylurea ("BZ 55") and the equivalent tolylsulphonylurea. Both reduced the blood sugar level in rats on oral administration and caused a sharp fall in the insulinase activity of the liver, the tolyl compound being the more potent. The anti-insulinase effect of the drugs was also demonstrated on liver extracts *in vitro*, the inhibition being non-competitive so that the drugs may act as enzyme poisons. It is concluded that the hypoglycaemic effect of these sulphonamides is due to inhibition of insulinase and a consequent decrease in the destruction of endogenous insulin. *C. L. Cope*

438. **Pregnancy and Diabetes Mellitus. A Clinical Study.** [In English]

L. HAGBARD. *Acta obstetricia et gynecologica Scandinavica* [*Acta obstet. gynec. scand.*] 35, suppl. 1, 1–180, 1956. 10 figs., bibliography.

439. **Clinical Aspects of Hyperinsulinism**

H. D. BREIDAHL, J. T. PRIESTLEY, and E. H. RYNEARSON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] 160, 198–204, Jan. 21, 1956. 17 refs.

The clinical features in 91 cases of hyperinsulinism seen at the Mayo Clinic during the years 1927 to 1953 inclusive are reviewed. The ages of the patients (47 males and 44 females) ranged from 9 to 72 years, but the maximum incidence of the condition occurred in the 4th, 5th, and 6th decades. In 76 cases an insulin-producing tumour of the pancreas was present—metastasizing carcinomata in 7, Grade-1 adenocarcinomata in 23, and adenomata in 46. In the remaining 15 cases no tumour of the pancreas was found either at operation or at necropsy. A history of diabetes in a close blood-relation was obtained in 15 out of 63 cases in the series, but none of the patients with hyperinsulinism had previously been diabetic.

In the majority of cases symptoms had been present for at least a year before the condition was diagnosed. Symptoms of hypoglycaemia were provoked by fasting or exercise or a combination of these, and most commonly occurred either in the early morning or in the afternoon when a meal had been missed and exercise taken; they were relieved by administration of glucose. In most cases the blood sugar level was below 40 mg. per 100 ml. during a hypoglycaemic attack. The glucose tolerance test was of little help in diagnosis; the blood sugar levels during a prolonged fast were, however, of considerable diagnostic value, only one patient with a tumour being able to fast for more than 48 hours without an attack of hypoglycaemia. Neurological complications included a distal progressive muscular atrophy secondary to motor neuronitis in 7 patients, residual hemiparesis in 2, and mental deterioration in 6.

Surgical treatment included excision of an islet-cell tumour in 48 cases, partial pancreatectomy in 26, and total pancreatectomy in 3. In 6 cases biopsy of a carcinoma was carried out. The presence of a tumour was recognized at the first operation in 64 of the 76 cases, in resected pancreatic tissue in 7, at a second operation in one case, and at necropsy in 4 cases. Postoperative hyperglycaemia occurred in 17 out of 48 patients in whom a tumour was excised locally and in 15 out of the 26 subjected to partial pancreatectomy, but in none of these cases did it last for more than a fortnight. There were 7 postoperative deaths in the entire series, but only one death occurred among the last 46 cases.

The authors consider the results of their investigation to indicate that at least 70% of patients with hyperinsulinism may "expect cure after the first operation", and that the recurrence rate after apparent cure is only 3%. *Charles Rolland*

ADRENAL GLANDS

440. **The Diagnostic Value of Plasma and Urinary 17-Hydroxycorticosteroid Determinations in Cushing's Syndrome**

A. E. LINDSAY, C. J. MIGEON, C. A. NUGENT, and H. BROWN. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 15–22, Jan., 1956. 3 figs., 18 refs.

The metabolism of 17-hydroxycorticosteroids was studied at the Veterans Administration Hospital (University of Utah College of Medicine), Salt Lake City, in 3 cases of Cushing's syndrome, due respectively to carcinoma, adenoma, and bilateral hyperplasia of the adrenal cortex. Plasma 17-hydroxycorticosteroids were estimated by the method described by Eik-Nes *et al.* (*J. clin. Endocr.*, 1953, **13**, 1280), urinary 17-hydroxycorticosteroids by the method of Glenn and Nelson (*J. clin. Endocr.*, 1953, **13**, 911), and urinary 17-ketosteroids by a modification of the method of Callow *et al.* (*Biochem. J.*, 1938, **32**, 1312).

Urinary 17-ketosteroid excretion was normal in the patient with an adenoma, increased slightly in the case with bilateral hyperplasia, and increased greatly (to over 200 mg. per 24 hours) in the patient with an adrenocortical carcinoma which had metastasized widely. In all 3 cases the fasting plasma level and 24-hour urinary excretion of 17-hydroxycorticosteroids were consistently increased. There was no significant difference in plasma level of 17-hydroxycorticosteroids between the 3 cases, none of which showed the diurnal variation—high in the morning and low in the evening—observed in normal subjects.

The intravenous infusion of 25 mg. of corticotrophin (ACTH) over 6 hours produced a negligible increase in the urinary excretion of 17-ketosteroids in the neoplastic cases, with a more obvious increase in the case of hyperplasia. On the other hand it caused an approximately fourfold increase in the plasma level and a threefold increase in the urinary excretion of 17-hydroxycorticosteroids in the 2 non-malignant cases, while the patient with adrenocortical carcinoma showed no increase in corticosteroid production. It is pointed out that the percentage increases in the 2 former cases were very similar to those seen in normal subjects, although the levels attained were very much higher.

The adenoma was excised and the patient with adrenocortical hyperplasia underwent bilateral subtotal adrenalectomy, with improvement in the clinical state in each case, although the latter patient required maintenance therapy with hydrocortisone subsequently.

H.-J. B. Galbraith

441. **Addison's Disease Associated with Histoplasmosis. Report of Four Cases and Review of the Literature**

K. R. CRISPELL, W. PARSON, J. HAMLIN, and G. HOLLIFIELD. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 23–29, Jan., 1956. 20 refs.

The association of Addison's disease with systemic histoplasmosis in 4 cases is reported from the University of Virginia Hospital, Charlottesville. All the patients had lived for some time in the Central Mississippi Valley, in which region occur the vast majority of the cases of histoplasmosis seen in the U.S.A. The diagnoses were made concurrently in one case, in one Addison's disease was diagnosed first, and in the other 2 the mycotic infection was diagnosed first. The diagnosis of histoplasmosis was made by biopsy of an oral lesion and by urine culture in one case, by biopsy alone in 2 (the lesions being in a vocal cord in one and the epiglottis in the other), and from suggestive changes in the radiograph of the chest and in the histology of a lymph node in the fourth. In the only fatal case necropsy showed destruction of the adrenal tissue by caseating granulomata which contained organisms resembling *Histoplasma capsulatum*. The authors regard the results of skin and complement-fixation tests as being of little value in the diagnosis of histoplasmosis compared with demonstration of the organism by culture or by histological examination of infected tissue.

At necropsy in cases of histoplasmosis the adrenal glands are among the organs most frequently involved, and at least 15 cases of this condition with symptoms suggestive of adrenal insufficiency have been reported previously. *H.-J. B. Galbraith*

The Rheumatic Diseases

RHEUMATIC FEVER

442. Application of the Antistreptolysin-O Titer in the Evaluation of Joint Pain and in the Diagnosis of Rheumatic Fever

S. B. Roy, G. P. Sturgis, and B. F. Massell. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 95–102, Jan. 19, 1956. 7 figs., 16 refs.

The importance of joint pain as a manifestation of rheumatic fever was evaluated in 648 consecutive patients under the age of 17 admitted to the House of the Good Samaritan (Harvard Medical School), Boston, between 1943 and 1948; cases of chorea were excluded from the study. On the criteria adopted (objective signs in two or more joints) significant arthritis was present in 50% of the patients, and of these joint pain was the presenting symptom in 94%, while cardiac involvement occurred in 50%.

The distribution of the antistreptolysin-O titres was studied in each of four clinical groups in order to determine its value in differentiating the joint pain due to rheumatic fever from that due to other diseases. The patients with rheumatic fever were divided into two groups: (1) 208 patients with definite rheumatic carditis, and (2) 227 patients with definite rheumatic fever and arthritis. In these two groups the antistreptolysin-O titres showed a similar distribution, namely, 400 units or more in 82% of Group 1 and in 85% of Group 2, and 159 units or less in 3 and 1·8% respectively. In Group 3, which contained 75 cases of juvenile rheumatoid arthritis, the titre was 400 units or more in 28% and 159 units or less in 56%. Group 4, composed of 92 patients with miscellaneous diseases of which joint pain was a prominent feature, showed a titre of 400 units or more in 8% and one of 159 units or less in 59·8%.

It is concluded that joint pain is a frequent, early, and important manifestation of rheumatic fever and that, while a high antistreptolysin-O titre is consistent with, but not diagnostic of, rheumatic fever, a very low titre may be regarded as excluding active rheumatic fever. The authors add that the height of the antistreptolysin-O titre affords no help in the prediction of heart damage.

F. T. Shannon

443. Therapeutic Effects of ACTH and Cortisone in Rheumatic Fever: Cardiologic Observations in a Controlled Series of 100 Cases

T. N. Harris, S. Friedman, H. L. Needleman, and H. A. Saltzman. *Pediatrics* [*Pediatrics*] **17**, 11–28, Jan., 1956. 27 refs.

A controlled investigation was undertaken of the efficacy of ACTH and cortisone in the treatment of rheumatic fever in 100 consecutive patients, aged 3 to 17 years, seen at three hospitals in Philadelphia between September, 1950, and June, 1954. The patients were divided into 3 groups: Group 1, without carditis, 21 patients; Group 2, an initial episode of carditis, 48 patients; and Group 3, recurrent carditis, 31 patients. Within each of these three clinical groups the patients were assigned in rotation to one of three treatment groups—ACTH, cortisone, and control (symptomatic treatment only). ACTH was given intramuscularly in a dosage of 40 mg. daily to children aged 3 to 4 years increasing with the age up to 120 mg. daily in those over 15 years of age. At first cortisone was administered intramuscularly in a dosage of 120 to 300 mg. daily according to age; later, a slightly larger dosage was given by mouth. During the first 48 hours all patients in the series received a larger dose than that determined by age. Hormone treatment was continued until all clinical evidence of activity had disappeared [the criteria of "activity" are not stated] and the erythrocyte sedimentation rate (E.S.R.) had remained at or below 15 mm. in one hour for at least a week; the dosage was then gradually reduced until the drugs were finally discontinued, usually after 8 to 10 days. Salicylates were not given to patients in the treated groups, and the dosage of such drugs in the control groups "was kept to a minimum" (less than ½ gr. per lb. (70 mg. per kg.) body weight daily). Injections of penicillin or sulphonamides were given prophylactically in all cases, and the hormone-treated patients received 1 to 2 g. of potassium citrate daily and a low-salt diet.

When the patients were discharged from hospital no significant differences were observed between the hormone-treated and control groups with carditis as regards the disappearance or persistence of murmurs or the appearance of new murmurs, the degree of transmission of apical systolic murmurs, or the duration of episodes of pericardial friction. [Dividing the patients into nine groups meant that there were very few in each group: the maximum was 17.] The appearance of new murmurs in the group without carditis initially was very exceptional. Changes in the pattern of the electrocardiogram and in heart size were so widely scattered within each treatment group that quantitative comparisons were not possible.

There were 2 deaths in the series: one control patient died after 6 weeks' illness, while another child, who was given ACTH for 6 weeks but showed "evidence of continued rheumatic activity", died 4 weeks after completing treatment. [The abstracter wonders whether these deaths could have been prevented by giving the benefit of specific treatment in the control case after it was apparent that there was no improvement, and by prolonging or changing treatment in the ACTH-treated case. In the latter, the criteria for the duration of treatment, as laid down by the authors, do not appear to have been observed.]

There was no difference in the response to hormone treatment, so far as cardiac murmurs were concerned,

whether treatment was started within one week or within 2 or more weeks of the onset of the disease. Rebound phenomena occurred in two-thirds of the cases when the drugs were withdrawn and were maximum in the second week; in one-half of these there was a rise in the E.S.R. only, while in the other half there were clinical signs as well. Serious intercurrent infections in the cortisone group included pyogenic meningitis (one case) in spite of daily prophylactic injections of penicillin. Hypertension developed in 13 of the hormone-treated patients and oedema, with or without ascites, in 21.

The authors found no evidence that the hormones, as administered, exerted a beneficial effect on the disease, particularly the cardiac manifestations; as they point out, however, the patients were observed only during the period in hospital and it is possible that benefits from such treatment may become apparent at a later stage. *John Lorber*

444. **Antistreptolysin and Streptococcal Antihyaluronidase Titers in Sera of Hormone-treated and Control Patients with Acute Rheumatic Fever**
T. N. HARRIS, H. L. NEEDLEMAN, S. HARRIS, and S. FRIEDMAN. *Pediatrics* [*Pediatrics*] **17**, 29–36, Jan., 1956. 2 figs., 18 refs.

A minimum of four samples of serum were taken from each of the patients with rheumatic fever included in the previous investigation (see Abstract 443), and their antihyaluronidase and antistreptolysin-O titres estimated, 2 being tested within 4 days of the patient's admission and 2 after an interval of one month. [For details of the methods employed the original paper should be consulted.] In the majority of patients receiving symptomatic treatment only there was no change in either titre after one month's interval, whereas in the majority of those given cortisone or ACTH there was a fall in both titres. The results are analysed by advanced mathematical methods. *John Lorber*

445. **The Prevention of Residual Endocarditis after Rheumatic Fever by Hormone Therapy.** (La prévention des endocardites résiduelles de la maladie de Bouillaud par l'hormonothérapie)
M. JEUNE and M. C. FAYOLLE. *Pédiatrie* [*Pédiatrie*] **11**, 69–77, 1956. 4 refs.

The authors state that although the effect of cortisone, ACTH (corticotrophin), and aspirin in preventing residual carditis following rheumatic fever has recently been shown to be about equal by workers in Britain and the U.S.A., it has been their experience at the Hôpital Debrousse, Lyons, that hormone therapy is definitely superior.

In an uncontrolled series of 83 cases of first attacks of rheumatic fever treated between October, 1951, and May, 1955, there were 31 without and 52 with cardiac involvement. The first 8 patients were given only one 15-day course of ACTH, but the remaining 75 were treated according to a fixed regimen, the dose of steroids being governed by the erythrocyte sedimentation rate (E.S.R.), determined twice weekly, the object being to reduce it as quickly as possible. The initial daily dose of ACTH given orally was 2 to 4 mg. per kg. body weight, this being equivalent to 4 mg. of hydrocortisone or 1 mg. of prednisone. If the fourth E.S.R. reading was still above 20 mm. in one hour the dose of ACTH was increased by 25 mg. daily; if it remained below 20 mm. on two consecutive occasions the dose was reduced by a similar amount. In this way a gradual reduction was effected, the total course usually lasting not more than 6 weeks in the most favourable cases, about 2 months in less favourable, and 4 months or more in the most serious cases. If the E.S.R. rose again after treatment steroid therapy was repeated. Concurrently, benzylpenicillin was given in weekly doses of 300,000 units together with 500 mg. of ascorbic acid and 1 g. of potassium chloride daily, bed rest being maintained for 2 weeks after the end of hormone administration.

In all, 71 children (7 out of the first 8 treated and 64 out of the remaining 75) were followed up for periods of from 6 to 36 months. Of these, 15 (6 from the former group) showed residual endocarditis. Of 40 patients whose treatment was started within 2 weeks of the onset of symptoms, only 4 had residual carditis, compared with 5 of the other 24, whose treatment was delayed. All 9 cases of endocarditis were in the group of 40 who had cardiac signs when treatment was started. There were no deaths in the series.

Thus the incidence of cardiac sequelae following hormone therapy was only 14%, compared with 70% in patients treated before hormone therapy was available. In the Anglo-American investigations mentioned above, in which no significant difference was found between the effects of hormones and aspirin, the dose of ACTH was only one-third of that employed in the present series. The authors thus suggest that although there has lately been a reduction in the severity and incidence of rheumatic fever, partly due no doubt to the use of antibiotics in acute tonsillitis, early admission to hospital and the institution of adequate hormone treatment are the factors most likely to reduce the risk of residual cardiac damage in this condition. *P. I. Reed*

446. **The Q–T Interval in Rheumatic Heart Disease**
L. KORNEL and K. BRAUN. *British Heart Journal* [*Brit. Heart J.*] **18**, 8–12, Jan., 1956. 1 fig., 19 refs.

A study of the Q–T interval in electrocardiograms (ECGs) from five groups of patients with rheumatic heart disease was made at the Rothschild Hadassah University Hospital, Jerusalem. In all, 164 tracings were examined from 157 subjects, the Q–T interval being corrected for cardiac rate ($Q–T_c$) by Taran and Szilagy's modification of Bazett's formula. Group I consisted of 33 normal subjects in whom the upper limit of $Q–T_c$ was 0·412 second. Group II consisted of 50 patients with active rheumatic heart disease, in all but 6 of whom the $Q–T_c$ was more than 0·412 second, ranging from 0·414 to 0·528 second. In Group III were 30 patients with "subclinical" rheumatic activity, and of these 28 had a prolonged $Q–T_c$ which varied from 0·415 to 0·468 second. Group IV consisted of 30 patients with quiescent rheumatic heart disease, in all but 2 of whom the $Q–T_c$ was below the upper limit of

normal. Group V consisted of 14 patients who had undergone mitral valvotomy, in 10 of whom the Q–T_c was prolonged; in 2 of these 10 cases Aschoff bodies were found on histological examination of the auricular appendage and in 2 others cellular accumulations resembling Aschoff bodies were seen, whereas in the 4 cases with a normal Q–T_c no histological evidence of activity was found.

The incidence of other abnormalities (P–R interval, S–T deviation, T changes) in the ECG in active cases was far below that of prolongation of Q–T_c. It is therefore concluded that an increased Q–T_c is a sensitive index of rheumatic activity. *C. Bruce Perry*

See also Microbiology and Parasitology, Abstract 303.

CHRONIC RHEUMATISM

447. **The Influence of an Early Artificial Menopause on Rheumatic Manifestations.** (De l'influence d'une ménopause artificielle précoce sur les manifestations rhumatismales)

J. FORESTIER and P. DE MARCHIN. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **22**, 819–823, Dec., 1955.

The authors question the acceptance of the term "menopausal rheumatism" for that chronic type of disease which appears about the age of 50 to 60 and is characterized by arthralgia, paraesthesiae, para-articular and painful "pre-arthrotic" manifestations (excluding the inflammatory types), and which is often attributed to alterations in endocrine balance, especially since oestrogens have been administered with success in these conditions.

The authors then report their observations on two groups of women aged 50 to 60: (1) 70 who had suffered early artificial menopause at the average age of 30 and who came under care for chronic rheumatism; (2) a control group of 200 non-castrated female patients attending the Hôpital de Bavière, Liège, for rheumatism. Among patients in Group 1 a short interval between the operation and onset of symptoms occurred in only 6 cases, the average age of onset in the others being 43½ and the average age at the first consultation being 50. In the control group the average age of natural menopause was 50, at onset of symptoms 46½, and at first consultation 54. Thus the influence of early artificial menopause upon the onset of chronic rheumatism appears to be slight.

Further, among 25 women with artificial menopause before the age of 40, there were 6 (28%) with rheumatism, while out of a random group of 100 normal control subjects 26 complained of rheumatism, with or without other disorders. Among 240 patients at Aix-les-Bains with the type of rheumatism in question, 21 reported onset before the age of 40, but only 2 of the total 240 had an early menopause, and in neither of these was there early onset of rheumatic symptoms.

The authors conclude that there is little evidence that rheumatic manifestations are due to lack of oestrogens, and suggest that arthralgia and paraesthesiae may be due to neurovegetative changes and vasomotor disorders which accompany the menopause, and the rheumatic, pre-arthrotic, and arthrotic lesions chiefly to the degenerative processes of ageing. *V. Reade*

448. **The Use of Hydrocortisone by Local Injection**

P. H. KENDALL. *Annals of Physical Medicine* [*Ann. phys. Med.*] **3**, 1–8, Jan., 1956. 1 fig., 15 refs.

The author reports the results obtained at Guy's Hospital, London, in 512 patients with joint and soft-tissue lesions treated by the topical injection of hydrocortisone. Affected joints were injected with 1 to 2 ml. of hydrocortisone (25 to 50 mg.) plus 1,000 units of hyaluronidase, but in the case of soft-tissue lesions 1 to 3 ml. of 2% procaine was substituted for the hyaluronidase in order to locate the lesion accurately and to give relief until the effect of the cortisone developed. Injections into tender areas around the shoulder joint were accompanied by injections into (1) the joint capsule, (2) the subacromial bursa, and (3) the long head of biceps.

Of 121 cases of rheumatoid arthritis, 75% showed "dramatic improvement" in symptoms and signs (plus increased range of movement) within 24 to 36 hours, such improvement lasting 7 to 10 days after each injection. The author considers the most suitable cases to be (*a*) those in which 1 or 2 joints are primarily affected, (*b*) those in which polyarticular affections have responded to general treatment with the exception of 1 or 2 joints, and (*c*) those in which cortisone or other drug therapy is being gradually withdrawn. In 36 cases of bilateral static osteoarthritis of the knee, however, the degree of improvement was no better than that in 36 control cases treated only with 2% procaine. On the other hand 41 cases of active inflammation (that is, those with minimal radiological changes in the joint or with aggravation of the osteoarthritis by injury) gave "far better results". Of 61 cases of acute periarthritis of the shoulder, 45 were completely relieved of symptoms and 13 improved within 7 to 14 days of injection. Of 23 cases of chronic periarthritis (showing chiefly fibrosis and impaired mobility), 13 recovered completely with the help of active assisted exercises in addition to the injections, in 4 to 6 weeks. Relief was also obtained in a high proportion of cases of traumatic synovitis (with or without haemarthrosis), tennis elbow, golfer's elbow, plantar fasciitis, De Quervain's syndrome, tenosynovitis, and traumatic arthritis of the elbow-joint.

Among the side-effects noted were a transient local urticaria (3 cases), local inflammation (2 cases), and a relatively mild, spontaneously-resolving, suppurative arthritis of the knee-joint. The author ascribes improvement in the acute cases to an "anti-inflammatory" effect, and tentatively suggests that improvement in chronic cases (for example, "frozen shoulder", "trigger finger") may be due to a fibrinolytic action. He states that the main value of hydrocortisone treatment in some of the above conditions is not so much in curing them as in appreciably hastening recovery—the principal aim of those concerned in rehabilitation. *M. Kendal*

449. **Inflammatory Rheumatism and Prolonged Treatment with Prednisone.** (Rhumatismes inflammatoires et traitements prolongés par la prednisone)
S. DE SÈZE, N. DEBEYRE, and P. BORDIER. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **72**, 216–226, Feb. 24, 1956. 1 ref.

The authors report the results obtained during a period of one year with prednisone in the treatment of 91 cases of rheumatoid arthritis and 91 cases of ankylosing spondylitis. In 28 cases in which no previous treatment with adrenocortical hormones had been given the response proved spectacular, 27 of these patients being able to resume a practically normal life taking a daily maintenance dose of 5 to 15 mg. In 57 cases the symptoms were already adequately controlled by maintenance therapy with cortisone or hydrocortisone, but in most of them further improvement was noted after changing to prednisone—certain residual inflammatory foci subsided and there was a concurrent fall in the erythrocyte sedimentation rate. The remaining 15 patients, who were receiving cortisone but had responded poorly, improved slightly when prednisone was substituted.

The reports of previous workers regarding the absence of side-effects with prednisone were not confirmed, the present authors finding the same precautions and strict medical supervision to be necessary as with cortisone. "Moon-face" developed in 55 cases, and observations on 2 patients suggested that this was likely to result from any relaxation of the salt-free diet, even when the dose of prednisone was only of the order of 10 mg. daily. Generalized capillary vasodilatation leading to erythema was noted in 45 cases, acne in 4, increased capillary fragility in 15, and hypertension in 26. Psychic disturbances—especially insomnia—tachycardia, and over-excitability were repeatedly noticed, as were hyperglycaemia and gastric disturbances.

H. F. Reichenfeld

450. **Prednisone in the Treatment of Rheumatoid Arthritis**
A. COHEN, R. TURNER, and R. DUNSMORE. *New England Journal of Medicine* [*New Engl. J. Med.*] **253**, 1150–1152, Dec. 29, 1955. 10 refs.

Thirty-three patients with severe rheumatoid arthritis were treated with prednisone, a new steroid with adrenocortical activity. The daily dosages ranged from 30 to 60 mg. initially to a daily maintenance dosage of 12·5 to 20 mg. A potency ratio of 3 : 1 or 4 : 1 as compared with cortisone was established. Objective improvement with a decrease in joint pain, tenderness and swelling and an increase in range of motion of affected joints occurred rapidly after the initiation of prednisone therapy. A significant decrease occurred in eosinophil counts and a moderate decrease in elevated erythrocyte sedimentation rates. Hypertension was augmented in one patient with essential hypertension, but hypertension in another caused by cortisone was relieved during prednisone administration. Prednisone had no adverse effects on blood sugar, serum sodium and potassium, or blood urea nitrogen levels. No patient had evidence of edema, and no glycosuria developed. One patient had a slight loss in body weight, one had a definite euphoria, and 4 had slight rounding of the face. A chronically scarred duodenal cap in one patient was adversely affected during 5 months' administration of prednisone by virtue of a pylorospasm.—[Authors' summary.]

451. **Prednisone and Prednisolone Therapy in Rheumatoid Arthritis. Clinical Evaluation Based on Continuous Observations for Periods of Six to Nine Months**
E. W. BOLAND. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 613–621, Feb. 25, 1956. 6 figs., 11 refs.

The recently introduced synthetic steroids prednisone and prednisolone were administered to 141 patients suffering from severe active rheumatoid arthritis. The series included a group of 32 patients not previously treated and these were given the steroids as initial treatment in oral doses of 10 to 20 mg. daily. For all patients the dosage was gradually reduced to maintenance levels by decrements of 1·25 to 2·5 mg. at intervals of 5 to 14 days. In most cases subjective relief was recorded within 24 hours, and objective improvement could be measured after 2 to 4 days. During a period of observation ranging from 6 to 9 months satisfactory improvement was maintained in more than 50% of the patients. It was considered that larger doses of hydrocortisone would have been necessary in order to produce similar results, and this impression was confirmed by the results in patients given prednisone and prednisolone who had previously been treated with hydrocortisone.

However, most of the patients experienced untoward reactions, notably ecchymotic skin lesions, vasomotor symptoms, and digestive complaints; on the other hand there were few cases of oedema and in no case was there evidence of hypertension or potassium loss.

As shown by biological experiments prednisone and prednisolone exhibit an adrenocortical hormonal activity which is 3 to 4 times greater than that of their analogues, cortisone and hydrocortisone. It would appear, therefore, that in the treatment of rheumatoid arthritis prednisone and prednisolone are to be preferred to hydrocortisone, except for patients with peptic ulcer and those in whom gastric irritation results from the administration of the new steroids, which provoke the secretion of about twice as much free hydrochloric acid as does hydrocortisone.

A. Garland

452. **Pleural Effusion Complicating Rheumatoid Arthritis**
P. A. EMERSON. *British Medical Journal* [*Brit. med. J.*] **1**, 428–429, Feb. 25, 1956. 28 refs.

In this paper from the Brompton Hospital, London, the author describes the cases of 6 patients who suffered from polyarthritis of the rheumatoid type and who, in exacerbations of their disease, developed pleurisy with effusion. The patients were thoroughly investigated to exclude other causes of pleurisy, and during a period of observation ranging from 2 to 4½ years none of them has

shown any clinical, radiological, or laboratory evidence to suggest any cause for the effusions other than the rheumatoid process. The effusions were found to be very persistent; in 2 cases they were still present after 2 years.

In the author's view these pleural effusions were due to involvement of the pleura in the rheumatoid process.

J. Warwick Butler

453. **Viscosity Studies on Hyaluronic Acid of Synovial Fluid in Rheumatoid Arthritis and Osteoarthritis**

E. Fletcher, J. H. Jacobs, and R. L. Markham. *Clinical Science* [*Clin. Sci.*] **14**, 653–660, Nov., 1955. 7 figs., 13 refs.

A detailed study of the viscosity (measured by capillary viscometry) and hyaluronic acid content of synovial fluid is reported from the Royal Free Hospital, London, with special reference to the complexity and polymerization of the hyaluronic acid molecule. Previous assumptions that a higher degree of polymerization exists in the effusions of rheumatoid arthritis than in those of osteoarthritis were not substantiated.

Values for anomalous viscosity were derived from estimations of specific viscosity under two different degrees of stress at the wall of the capillary as an index of the molecular complexity of the hyaluronic acid molecule. [The formula employed includes a possible source of error in the form of a mean value for the specific viscosity of fluids showing no anomaly.] The limiting viscosity of Sundblad (*Acta Soc. Med. upsalien.*, 1953, **58**, 113) was also determined and his findings confirmed. Hyaluronic acid glucosamine was isolated by Sundblad's method and estimated colorimetrically with Ehrlich's reagent; emphasis is placed on the value of this method in obviating errors due to the interference of proteins and the inconstancy of dried precipitated mucin.

Statistical examination of the mean values obtained for 60 specimens of effusion from cases of rheumatoid arthritis and 20 from cases of osteoarthritis suggest that there is: (1) a similar range of polymer size in the two conditions; and (2) a higher mean value of specific viscosity in osteoarthritis, which could be explained by a higher concentration of hyaluronic acid in this condition.

Harry Coke

454. **Observations on the Effects of Intra-articular Phenylbutazone**

D. H. Neustadt and O. Steinbrocker. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **47**, 284–288, Feb., 1956. 8 refs.

From the Hospital for Joint Diseases, New York, the authors describe the results obtained with the intra-articular injection of phenylbutazone (" butazolidin ") in the treatment of 18 patients with rheumatoid arthritis, 11 with osteoarthritis, and 4 with allied rheumatic disorders. The drug (1 g. in a 20% solution containing also lignocaine) was injected at intervals of one to 6 weeks, the usual dose given being 3 to 5 ml. Both the subjective and the objective effects of the treatment were assessed, and in 10 cases with effusion weekly aspiration of the synovial fluid was carried out and changes in its cytology noted.

Beneficial results were particularly noticeable in the more acutely inflamed and painful joints with effusion, there being a concurrent decrease in the number of leucocytes in 5 cases within one to 2 weeks after the injections, while in a few cases in which fluid was aspirated 2½ days after the injection leucocytic disintegration was observed. This effect was similar to the action of phenylbutazone on synovial fluid *in vitro*. Of the 18 patients with rheumatoid arthritis (who received a total of 45 injections), 7 showed major improvement, 7 minor improvement, and 4 no improvement; while of the 11 with osteoarthritis (receiving 34 injections), marked improvement occurred in only one, slight to moderate improvement was noted in 7, and no improvement in the remaining 3.

There was no improvement in 4 miscellaneous cases, which included one case each of olecranon bursitis, swollen knee-joint in a patient with ankylosing spondylitis, tendovaginitis of the wrist, and Reiter's syndrome with an acutely swollen knee.

The possible mode of action of phenylbutazone as a specific anti-inflammatory agent is discussed.

H. F. Reichenfeld

455. **Hypophyseal Abnormities [*sic*] in Rheumatoid Arthritis**

A. G. E. Pearse. *Rheumatism* [*Rheumatism*] **12**, 29–36, April, 1956. 6 figs., bibliography.

456. **Intra-articular and Paravertebral Injection of Cortisone in Osteoarthritis of Spine**

A. Cohen, G. E. Scott, R. F. Turner, and I. Rose. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 1724–1727, Dec. 31, 1955. 2 figs., 15 refs.

At Philadelphia General Hospital cortisone acetate or hydrocortisone acetate was injected into the sacro-iliac joints or into tissue in the region of the cervical, thoracic, and lumbar vertebrae of 46 patients with osteoarthritis of the spine, on the assumption that the pathological process extends more widely than is shown by radiographic appearances. Up to 23 doses, each of 12·5 to 25 mg., were given, usually at intervals of one or 2 weeks. The technique of injection is described and illustrated with diagrams. Of the 46 patients, 37 received cortisone and 9 hydrocortisone; neither drug appeared to have any advantages over the other. The results were judged by subjective relief of pain.

Of the 26 patients with cervical osteoarthritis, 14 claimed to receive marked or moderate relief, while of 14 treated by sacro-iliac injection, 11 experienced such relief. (Similar figures were obtained later with a trial of prednisolone acetate in 22 comparable cases.) Generally, if no benefit was seen after four injections further attempts were of little avail.

[The authors' views on the role of heavy domestic work and other occupational factors in the aetiology of osteoarthritis require to be substantiated.]

J. N. Agate

Neurology and Neurosurgery

457. **The Neurological Complications of Behcet's Syndrome**

C. A. PALLIS and B. J. FUDGE. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] **75**, 1–14, Jan., 1956. 5 figs., 34 refs.

From the Royal Infirmary, Cardiff, the authors report 2 cases of Behçet's syndrome (relapsing iritis with genital and oral ulceration) in which neurological complications developed. The first patient, a man of 47 who had had recurrent iritis for 4 years and subsequently suffered from keratitis and recurrent ulceration of the genitalia, legs, and forearms, suddenly developed a spastic paraplegia. The protein content of the cerebrospinal fluid (C.S.F.) was more than 5 g. per 100 ml. and there was myelographic evidence of arachnoiditis. The second patient, a man of 44, had had recurrent oral and genital ulceration for 15 years and progressive stiffness of the limbs for 18 months. In this case there were mental deterioration, Parkinsonian features, nystagmus, gaze pareses, dysarthria, and a spastic tetraparesis. The C.S.F. contained 6 cells (3 polymorphonuclear leucocytes) per c.mm., and 90 mg. of protein per 100 ml.

The authors briefly review 11 published cases in which there were neurological complications; 4 of these cases (in young adults) proved fatal. They identify three patterns of nervous-system involvement—namely, a brainstem syndrome, a meningomyelitic syndrome, and an organic confusional syndrome (possibly encephalitic). The principal theories concerning the aetiology of the condition—whether it is vascular, allergic, or infective in origin—are discussed; the authors conclude that a virus aetiology is most probable. *John N. Walton*

458. **A Comparison of Hyperventilation and Apnoea Activation of the EEG**

D. SILVERMAN. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **8**, 41–48, Feb., 1956. 8 figs., 3 refs.

At the Graduate Hospital of the University of Pennsylvania, Philadelphia, 1,000 consecutive patients undergoing electroencephalography with routine activation by hyperventilation for 2 to 3½ minutes were instructed to hold their breath for as long as possible immediately after the period of overbreathing. In most cases 1½ minute of apnoea was required to produce a definite effect on the electroencephalogram (EEG), and 213 patients failed to hold their breath for a minimum of 1 minute and were therefore excluded from the series. In the remainder the responses to hyperventilation and to apnoea were compared and the results correlated with age, EEG classification, clinical diagnosis, and diagnostic value of the EEG.

In 311 cases no changes were seen in the EEG during hyperventilation, and in 480 none during apnoea. In the remainder the most common response to both procedures was a slowing in the 2- to 4-c.p.s. range which was usually, though not always, more marked on overbreathing. The degree of slowing produced by both procedures was inversely related to age, but slowing by itself is not usually considered to be pathological. Responses in the 5- to 7-c.p.s. range—focal slow or sharp waves and focal spikes, as well as paroxysmal discharges of different kinds—were also observed.

It is concluded that apnoea is a safe and simple activation procedure which may add useful information in a small but significant proportion of cases of suspected epilepsy, space-occupying lesions, and vascular and post-traumatic disorders. *William Cobb*

459. **Lumbar and Sacral Compression Radiculitis (Herniated Lumbar Disk Syndrome)**

D. MUNRO. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 243–252, Feb. 9, 1956. 5 figs., 4 refs.

The author discusses the diagnostic, clinical, pathological, operative, and postoperative aspects of lumbar and upper sacral compressive radiculitis, basing his observations on a series of 545 patients (402 men and 143 women) seen at the Massachusetts Memorial and City Hospitals, Boston. In his view the best contrast medium for myelography is " pantopaque ". The commonest cause of root compression is rupture of the intervertebral disk, but other lesions are also frequently encountered. A period of conservative treatment should be tried in all cases before operation. The author stresses the importance of adequate exposure and meticulous haemostasis at operation, which was performed in 375 cases with 4 deaths. The most frequent complication was development of a haematoma deep in the wound. Fusion of the vertebral column at the time of the first operation is considered to be absolutely contraindicated. The management of convalescence is described. (The long-term results are to be reported later.) *L. Crome*

460. **Statistical Studies of the Problem of Disseminated Sclerosis. II. The Clinical Picture.** (Statistische Untersuchungen zum Problem der Multiplen Sklerose. II. Das Krankheitsbild der Multiplen Sklerose)

L. ABB and G. SCHALTENBRAND. *Deutsche Zeitschrift für Nervenheilkunde* [*Dtsch. Z. Nervenheilk.*] **174**, 199–218, 1956.

From the University Neurological Clinic, Würzburg, the authors present a careful analysis of the clinical features of 1,420 cases of disseminated sclerosis. Most of the information was obtained from the clinical records and through postal inquiry, although 19% of the patients were personally examined. The sex incidence was approximately equal, and the commonest age of onset was between 20 and 30 years. The first subjective mani-

festation was visual disturbance in 21% of cases, paraesthesiae in 17%, motor disturbance in 14%, and double vision or dizziness and vomiting in a small proportion. The most frequent complaints in the subsequent stages were loss of balance, tiredness, headache, weakness in the arms, and stiffness in walking. The cerebrospinal fluid was obtained by cisternal puncture in 53·4% and by the lumbar route in 46·6%, no significant difference being found between the two groups; the fluid was normal in 52% of cases and had an increased protein content in 48%.

The prognosis in these cases seems to have been worse than that recently reported by McAlpine, for a life expectancy of over 10 years was found in only 42%.

G. S. Crockett

461. **Statistical Studies of the Problem of Disseminated Sclerosis. III. Aetiological Factors.** (Statistische Untersuchungen zum Problem der Multiplen Sklerose. III. Ätiologische Faktoren)

L. ABB and G. SCHALTENBRAND. *Deutsche Zeitschrift für Nervenheilkunde* [*Dtsch. Z. Nervenheilk.*] **174**, 219–234, 1956.

In a study of the aetiological factors involved in a total of 1,420 cases of disseminated sclerosis [see Abstract 460] the authors were unable to find convincing evidence of a familial disposition, only 29 out of 472 patients questioned (6·52%) having a relative with the disease. Manual workers were more commonly affected than any other occupational group, and seemed to develop a more rapidly progressive form of the disease. No definite nutritional factor in aetiology could be demonstrated. In 41·7% of 558 cases in which the point was investigated an infective condition had preceded the onset of neurological symptoms by less than 2 months, while trauma preceded the onset in 10·8% of 522 cases. Many patients had noted undue bodily fatigue or emotional disturbance shortly before the onset. Other possible aetiological factors which were investigated without any definite conclusions being drawn were inoculations, insect bites, exposure to poisons (such as lead), and contact with animals. Hot weather seemed to have a deleterious effect in quite a large proportion of cases.

[This painstaking statistical study, of which only a few of the findings can be mentioned here, should be read by all working to find an answer to the problems posed by this common and baffling nervous disorder.]

G. S. Crockett

462. **Clinical Evaluation of Ambenonium (Mysuran) Chloride**

M. R. WESTERBERG. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] **75**, 91–94, Jan., 1956. 1 ref.

The author has studied the efficacy of " ambenonium " (" mysuran ") chloride (N′:N′-bis-(2-diethylaminoethyl)-oxamide-bis-2-chlorobenzyl chloride) in 34 unselected cases of myasthenia gravis. In 26 cases the patient found the drug to be effective in increasing muscle strength. Compared with neostigmine it was 5 to 10 times more potent, its action being about equally rapid in onset but longer in duration. On the other hand 12 patients found ambenonium to be ineffective or its action to be accompanied by excessive side-effects, chiefly symptoms of overstimulation of the central nervous system or overactivity of the parasympathetic system. In this respect it was less toxic than neostigmine, but more toxic than pyridostigmine.

The author concludes that ambenonium is an effective agent in the treatment of myasthenia gravis, but recommends that it should be used cautiously on account of its great potency.

R. G. Rushworth

463. **Treatment of Myasthenia Gravis with Mestinon Bromide**

J. E. TETHER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 156–158, Jan. 21, 1956. 6 refs.

From his experience with " mestinon " bromide (a dimethyl carbamate of 3-hydroxy-1-methylpyridinium bromide) in the treatment of 165 patients with myasthenia gravis at the Indiana University Medical Center, Indianapolis, the author concludes that in the majority of cases it is preferable to neostigmine as it gives an effective, smooth control of myasthenic symptoms without distressing side-effects or wide fluctuations in the intensity of its action. In particular, his patients found that the effect of mestinon lasted better through the night than that of neostigmine.

J. W. Aldren Turner

BRAIN AND MENINGES

464. **Cerebral Hemispherectomy in the Treatment of Hemiplegia and Certain Infantile Encephalopathies.** (L'hémisphérectomie cérébrale dans le traitement de l'hémiplégie et de certaines encéphalopathies infantiles)

D. FEREY. *Presse médicale* [*Presse méd.*] **64**, 81–84, Jan. 18, 1956. 4 figs., 2 refs.

The author reviews 10 cases of infantile hemiplegia in which he has performed hemispherectomy since July, 1953. The aetiological factors represented were birth injury (5 cases), encephalitis of various kinds (4 cases), and trauma (one case). The author's indications for the operation are: severe and uncontrollable epilepsy, grave alterations of character, and severe mental deficiency; less important is the aim of improving the hemiplegia. It is stressed that full preparatory clinical and radiological investigation, including angiography and pneumoencephalography, must be carried out, since the presence of even slight atrophy in the hemisphere which is to remain is an absolute contraindication to the operation; hemispherectomy should also be refused if the hemiplegia is only minimal, if fits are occurring only infrequently, or if there are no associated personality changes. Only about one-third of all the author's cases of infantile hemiplegia were regarded as suitable for this radical operation. Of the 10 patients, 8 survived; 5 out of the 6 with epilepsy were freed from attacks, 6 with mental defect were improved, particularly in regard to power of attention, and in 5 out of the 8 cases the hemiplegia was improved.

J. B. Stanton

465. **Chronic Subdural Haematoma in Infancy.** (L'hématome sous-dural chronique du nourrisson)
M. LELONG, F. ALISON, J. ROUGERIE, LE TAN VINH, and R. CALDERA. *Archives françaises de pédiatrie* [*Arch. franç. Pédiat.*] **12**, 1037–1084, 1955. 17 figs., bibliography.

From the Hôpital St. Vincent-de-Paul, Paris, the authors present a detailed study of 31 cases of chronic subdural haematoma in children, of which 12 were operated upon and 2 subjected to post-mortem examination. In addition, the morbid anatomical findings are described in 4 cases not recognized during life, but discovered post mortem. The children (17 boys, 14 girls) ranged in age from 4 days to 2 years, 29 being in the first year of life, with a marked preponderance between the 4th and 9th months. In 4 cases trauma at birth was indisputable, and in 4 others it was possible, but apart from these the cause of the subdural haematoma was not obvious, though malnutrition was a feature of many of the cases.

On lumbar puncture a normal fluid was obtained in 23 cases and it is pointed out that subdural puncture alone can confirm the existence of a subdural haematoma. The necessity of performing puncture of the fontanelle in all cases of abnormal increase in the size of the head in infancy is stressed. In 22 cases the lesion was bilateral, in 8 it was unilateral, and in one puncture was not practicable. Bilateral retinal haemorrhages were seen in 10 cases, in one of which the haematoma was unilateral; and unilateral retinal haemorrhage (always on the right) in 3 cases, although the haematoma was bilateral. The results of encephalography are difficult to interpret, but cerebral arteriography permits site, amount, and extent of the effusion which separates the brain from the cranium to be determined accurately, and was carried out in 9 cases in this series. Careful anatomical dissection of the brain post mortem, when this has been made possible by the adoption of a technique whereby the brain is removed with its membranes intact, shows that the haematoma is always intradural rather than subdural.

All the patients were given a corrected and balanced diet, with added vitamins and calcium, and 10 of the patients—for the most part the older ones—received only such general treatment; a good result was obtained in 2 of these and an unfavourable result in 5, while 3 could not be followed up. Three of the patients received radiotherapy in addition, with a " relatively favourable " result in one case only. The remaining 18 patients were treated either by repeated puncture of the fontanelle or by surgical intervention. Attention is drawn to the importance of not delaying the puncture and of judging correctly the right moment when the case should be placed in the care of a neurosurgeon. It is also emphasized that these haematomata recur persistently, and a single evacuation is frequently not sufficient. The results of surgery were as follows: (1) repeated puncture was carried out on 6 patients (2 of whom could not be followed up) with a favourable result in one case and unfavourable in 3 (2 of these children developed hydrocephalus); (2) of 7 patients treated by drainage (2 of whom could not be followed up) the result was favourable in 4 and unfavourable in one; (3) 5 patients were treated by resection, 3 with favourable and 2 with unfavourable results, one of the latter cases being fatal and persistent hemiparesis occurring in the other.

The essential features of all the cases are given in tabular form. *D. P. McDonald*

466. **Chronic Cerebral Hypertensive Disease**
W. HUGHES and P. K. G. WARREN. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **4**, 8–17, Jan., 1956. 9 refs.

The authors, writing from Stapleton Hospital, Bristol, amplify the concept of " chronic cerebral hypertensive disease ", as embodied in a previous publication (Hughes *et al.*, *Lancet*, 1954, **2**, 770; *Abstracts of World Medicine*, 1955, **17**, 142). They describe a syndrome with the features of " a chronic disease characterised by sustained arterial hypertension, multiple strokes, emotional lability, pseudo-bulbar palsy, and mental deterioration ", in which the chief post-mortem findings are " ischaemic lesions particularly concentrated in the distribution of the long perforating branches of the middle and anterior cerebral arteries ".

[One of the essential components of the syndrome as defined is hypertension. But, in fact, all the clinical and pathological features are not uncommonly to be seen in geriatric practice quite independently of hypertension. It is doubtful, therefore, whether this syndrome can properly be regarded as a disease entity.]

P. D. Bedford

EPILEPSY

467. **Kojevnikov's Syndrome (Continuous Partial Epilepsy).** (Le syndrome de Kojevnikoff. (Épilepsie partielle continue))
H. HECAEN and J. F. DEREUX. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **32**, 545–553, Feb. 14, 1956. 1 fig., 3 refs.

The syndrome of Kojevnikov, or continuous partial epilepsy, is a rare clinical entity which consists in an association of continuous unilateral myoclonic movements (usually confined to the distal segment of one limb) with recurrent Jacksonian convulsions, both affecting the same side of the body. The authors review the history of the syndrome, analyse 99 cases collected from the literature, and add detailed descriptions of 4 cases seen personally. On this basis they discuss the clinical manifestations of the syndrome, its pathogenesis, and the electroencephalographic (EEG) and electromyographic changes accompanying it.

They suggest that the syndrome should not be classified with the myoclonic epilepsies, but should rather be regarded as a variant of Jacksonian epilepsy, possibly with multiple aetiology, but with localization to the contralateral cerebral hemisphere. They point out, however, that the condition differs from Jacksonian epilepsy proper because its clinical manifestations cannot be explained by any purely cortical excitatory process. They reason that the excitation must arise from two different levels, namely, cortical (focal seizures) and sub-

cortical (myoclonic movements), though not necessarily from two different lesions. So just as a single lesion may affect both levels at once, or begin at one level and then spread to the other, so the clinical picture may be complete from the beginning, or at first dissociated and only later acquire the other component. In support of this theory they advance the following main arguments. (1) The syndrome is rare, in contrast to focal epilepsy, which is common. (2) The absence of a constant temporo-spatial correlation between the EEG and electromyographic recordings and the absence of any EEG abnormalities in some cases suggest that abnormal thalamo-cortical connexions may be the fundamental lesion. (3) The fact that symptomatic therapy, including decortication, may control the focal seizures without modifying the myoclonic movements [but this dissociation is difficult to reconcile with the assumption that only one cortical lesion is causing the syndrome].

[This is an interesting and closely argued article. The figure reproduced shows a simultaneous electroencephalographic and electromyographic recording of one of the authors' cases. It is unfortunate that only 3 references are given, although many more sources are mentioned in the text.] *Marcel Malden*

468. **Primidone (Mysoline) in the Treatment of Epilepsy. Results of Treatment of 486 Patients and Review of the Literature**

S. LIVINGSTON and D. PETERSEN. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 327–329, Feb. 16, 1956. 27 refs.

The authors report, from Johns Hopkins Hospital, Baltimore, their experience with primidone (" mysoline ") in the treatment of 486 patients with various types of epilepsy, of whom 294 had been taking full doses of other anticonvulsants without achieving adequate control. These latter patients were given primidone in addition to their previous medication, while the remaining 192 patients, who had had no previous treatment, received primidone only. The dosage ranged from 375 mg. to a maximum of 500 mg. four times a day.

The drug was effective only in cases of grand mal, there being no improvement in patients with petit mal or psychomotor or minor motor attacks. The major attacks were completely controlled in 57% of the previously untreated patients and in 28% of those who had obtained partial relief from other anticonvulsants. Notably, the seizures were well controlled in 4 of the 23 patients who had been entirely refractory to maximum doses of these other drugs. Of the side-effects, which occurred in 160 (33%) of the cases, drowsiness was the most prominent, but in 127 cases this disappeared spontaneously within a few weeks of onset and treatment was not interrupted; however, in 33 patients the lethargy was so severe that the drug had to be discontinued. Dizziness was reported in 22 cases and ataxia in 19, and in 9 and 4 of these respectively treatment had to be stopped.

[The authors thus confirm the general impression that primidone is of value in grand-mal epilepsy, though its side-effects limit its usefulness.] *N. S. Alcock*

469. **Further Evaluation of Acetazolamide (Diamox) in Treatment of Epilepsy**

C. T. LOMBROSO, D. T. DAVIDSON, and M. L. GROSSI-BIANCHI. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 268–272, Jan. 28, 1956. 1 fig., 16 refs.

The induction of acidosis by various means has been accepted as a useful form of treatment in epilepsy. The introduction some 3 years ago of acetazolamide (" diamox "), which inhibits carbonic anhydrase throughout the body, suggested to the authors that it might be useful in the treatment of epilepsy, and in this communication from the Children's Medical Center (Harvard Medical School), Boston, they report on its use in 126 cases, in all of which previous therapy had been ineffective; 82 patients were under 12 years of age, 24 between 12 and 19, and 20 were aged 21 or more. The dosage ranged from 8 mg. to 30 mg. per kg. body weight daily, the drug being administered in tablets of 100 mg. or 250 mg. twice or three times daily with meals. The period of observation was up to 3 years and in no case was it less than 3 months. The seizures were of petit-mal type in 29 cases, petit mal and other types in 41, and other than petit mal in 56 cases.

The number of seizures was reduced by 90% in 37% of the cases, by 50 to 90% in 17%, and by 50% or less in 46%. Diuresis occurred, but was not prolonged in any case. It was not possible to correlate improvement with the type of epilepsy, a family history of the disease, or a history of brain damage. Maximum improvement occurred in those cases in which alkalosis induced by hyperventilation produced maximal increase in spike-wave discharges in the electroencephalogram. No serious side-effects were noted, and no patient was worse after treatment. The authors consider that the beneficial effects of acetazolamide may be due to acidosis or to dehydration, or they may be the result of specific inhibition of carbonic anhydrase in the neurones. They are cautious in their conclusions, but consider that the drug should prove a useful adjunct in the treatment of epilepsy. *William Hughes*

470. **Experience with the Surgical Treatment of Psychomotor Epilepsy. Early Results**

J. A. PICAZA and J. GUMÁ. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] **75**, 57–61, Jan., 1956. 11 refs.

The authors' experience in the surgical treatment of 34 cases of psychomotor epilepsy at the Hospital Mercedes, Havana, Cuba, is recorded. The results after follow-up for periods up to 4 years are classified according to the criteria of Penfield and Steelman and compared with those of other authors; the similarity of all these figures is noted.

In 20 cases the treatment was regarded as successful, there being complete or almost complete freedom from attacks after operation. The best results were obtained in traumatic cases, those in which a definite lesion was found on macroscopical or histological examination of excised brain tissue, and those in which radical temporal lobectomy was carried out. *R. G. Rushworth*

Psychiatry

471. **The Nature of Rhythm Studied Experimentally in Deaf and Normal Subjects.** (Das Wesen des Rhythmus im Experiment an Gehörlosen und Normalsinnigen) H. FELDMANN. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **194**, 36–61, 1955. 4 figs., 40 refs.

The ability to reproduce rhythms presented by visual, vibratory, and auditory means was tested at the Free University, Berlin, in 50 completely deaf subjects aged 6 to 17 years and in 20 healthy subjects. Tests were carried out in comparable conditions with and without the possibility of sensory control. The rhythms were reproduced by the subject by means of a telegraphist's key and recorded by a kymograph, and the results were evaluated statistically.

The following are some of the author's findings. The deaf are not inferior to other persons in their sense of rhythm and the ear is not superior in the perception of rhythmic stimulation to other sensory organs if tested under comparable conditions. The production of rhythm as an active performance is not dependent on control by the higher senses acting as a feed-back mechanism. The more complicated rhythms can be reproduced by normal children only after the age of 6 to 7 years and by the deaf-mute after the 10th or 11th year; younger subjects can reproduce only regular tappings. A period of time can be perceived and reproduced as a temporal whole up to the length of 1·4 to 1·5 second, a longer period being delimited as the sum of smaller periods. The sense of time or rhythm is identical for all conscious psychological events.

On the basis of the elaborate and original experimental work reported in this paper the author puts forward a new theory of the neurophysiology of rhythm.

W. Mayer-Gross

472. **Rhesus Incompatibility and Mental Deficiency** L. CROME, B. H. KIRMAN, and M. MARRS. *Brain* [*Brain*] **78**, 514–536, 1955. 39 refs.

The authors describe 9 cases of mental deficiency associated with Rh incompatibility and neonatal jaundice occurring among 800 mentally defective patients at the Fountain Hospital, London, during the last 6 years. As an indication of the comparative frequency of the condition they report that 20 cases of phenylketonuria and 150 of mongolism were noted during the same period.

The authors believe that the syndrome of bilateral athetosis, deafness, and mental retardation is the result of brain damage due to Rh incompatibility. The history usually includes severe neonatal jaundice, hypertonicity, and occasionally convulsions, followed by apparent improvement, but later, involuntary incoordinated movements may be observed. The authors emphasize, however, that this "typical" syndrome is very variable, and in fact was complete in only one of the 9 cases described. They suggest that further criteria, such as potentially incompatible blood groups as between mother and child, specific antibodies in the mother's serum, and a previous pregnancy or incompatible transfusion must be looked for. But even these criteria do not invariably justify the conclusion that the condition is due to blood-group incompatibility, since other conditions, such as mongolism, may be associated with them. In the cases coming to necropsy widespread loss of cells in the cerebral cortex and a more localized degenerative change in the globus pallidus were found but, as the authors point out, these changes are often seen post mortem in low-grade mental defectives. The electroencephalogram may be relatively normal, in spite of gross interference with motor activity.

The authors suggest that the brain damage could probably have been prevented in some of these patients who were healthy at birth if exchange transfusion had been performed; 3 of them, however, were born before the rhesus factor was discovered. In the education of such patients—only 3 of them were potentially educable—special regard should be paid to the deafness and the motor handicap, and a very high ratio of staff to pupils is required for the necessary individual attention. In the authors' experience the various forms of therapy for which claims have been made seem to have no special value, nor have muscle relaxants or surgery generally been of help.

G. de M. Rudolf

473. **Reproducible Psychogenic Attacks of Asthma** E. DEKKER and J. GROEN. *Journal of Psychosomatic Research* [*J. psychosom. Res.*] **1**, 58–67, Feb., 1956. 9 figs., 15 refs.

Tests were carried out at the Wilhelmina Gasthuis, Amsterdam, on 12 patients with bronchial asthma [selected on unspecified grounds from a total of 31] to determine the effect of psychological stimuli on respiratory function as measured by the vital capacity. The emotional stimuli used were selected with reference to the individual's history.

According to their reactions the patients fell into three groups: (1) 6 patients showed no reaction; (2) 3 showed minor reactions; and (3) 3 patients developed frank asthmatic attacks. In a number of cases it was clear that the asthmatic attacks were associatively related to traumatic life experiences, and the clinical picture of the experimental attacks was indistinguishable from that of spontaneous attacks or those provoked by allergens. Five of the 6 patients who showed no response stated that the situation was not sufficiently realistic, while the sixth was surprised at her lack of response. It was found that a high intensity of emotion was not in itself sufficient to provoke an attack, but must be associated with a specific sensory stimulus such as a particular smell

or the presentation of some object associated with a traumatic episode. Thus the emotional stimulus " must not only have a certain intensity . . . but also be of a more or less specific quality ". Many of the patients reported trauma, phantasies, or dreams after exposure to the asthmogenic situation, and it is suggested that this procedure may have an application as a form of therapeutic abreaction. Two of the patients also reacted to the inhalation of one or more common allergens, and the authors therefore regard as unjustified the division of asthma into " psychic " and " allergic " categories.

J. L. Standen

474. **Deliberate Disability**

J. R. HAWKINGS, K. S. JONES, M. SIM, and R. W. TIBBETTS. *British Medical Journal* [*Brit. med. J.*] **1**, 361–367, Feb. 18, 1956. 2 figs., 18 refs.

The authors draw attention to certain patients who perpetrate deliberate deceits in the medical sphere, but in whom, unlike most malingerers and many hysterics, the disability created or simulated " is not directed to immediate material gain or advantage ". There is a close resemblance between this type of patient and patients suffering from anorexia nervosa, and it was felt that further study might throw some indirect light on the latter condition.

In a series of 19 such cases of deliberate disability seen at the United Birmingham Hospitals during the 3-year period 1952–5, all but 3 of the patients were female and all but one unmarried. The age at onset lay between 17 and 32. Only one patient was below average intelligence, and while emotional immaturity was almost universal, all but 5 were of dynamic and effective personality. Of these 5, 2 were males whose cases were distinguished by features of psychopathic personality. Obsessional traits were frequently present. The systemic distribution of symptoms was diverse, simulated pyrexia, swelling of an arm from constricting bands, and dermatitis artefacta being the most common, with " neurological " lesions also prominent. It seemed significant that a high proportion of the patients had some medical association; 10 were nurses, 3 did voluntary spare-time nursing, and one had other hospital employment, while the non-psychopathic male was married to a nurse.

Although no adequate psychopathology was elicited in several cases, the authors suggest that disturbance in parent–child relationships was a more important causative factor than the prospect of immediate secondary gain. The parallel with anorexia nervosa in respect of such characteristic features as female predominance, similar age range, single status, immature but not inadequate personality, and a background of unsatisfactory childhood relationships, with little or no immediate secondary gain, is stressed by the authors and it is pointed out that deliberate deceits, such as self-induced vomiting and concealment and disposal of food, are frequently practised by patients with anorexia nervosa. The diagnosis and prognosis are discussed and suggestions for treatment are made.

[The authors recognize that " many might . . . challenge the usefulness of distinguishing this group of patients from conversion hysteria", but they do not appear to provide a convincing reason for making such a distinction.] *J. MacD. Holmes*

475. **The Sedation Threshold as an Objective Index of Manifest Anxiety in Psychoneurosis**

C. SHAGASS and J. NAIMAN. *Journal of Psychosomatic Research* [*J. psychosom. Res.*] **1**, 49–57, Feb., 1956. 5 figs., 9 refs.

The " sedation threshold " is defined as the amount of soluble amylobarbitone, injected intravenously, which is needed to produce certain quantitative changes in the electroencephalogram (EEG), associated with the onset of slurred speech. In an investigation carried out at McGill University, Montreal, of its validity as an index of manifest anxiety, the sedation threshold was determined in 121 psychoneurotic patients and the values compared with those obtained in 45 healthy control subjects. The mean threshold for the control subjects was 3·09 mg. per kg. body weight and that for the patients 4·15 mg. per kg., the difference being statistically significant ($P < 0.001$); moreover, the control values showed a much narrower range of variation. The mean thresholds for different diagnostic groups were then determined and showed close correlation with the degree of clinically manifest anxiety present, the groups, arranged in ascending order of threshold, being: hysteria, mixed neurosis, anxiety hysteria, obsessive-compulsive neurosis, neurotic depression, and anxiety state; most of the differences in mean threshold between the groups were significant. Repeat tests on 20 patients after intervals of 3 to 400 days showed that the threshold was stable, and a further check showed previous sedation to have no effect on the threshold. The procedure is therefore regarded as satisfying the necessary criteria of validity as an objective means of measuring manifest anxiety.

The authors emphasize that the time and skill necessary for recording and interpreting the EEG limit the possibilities of using the procedure as a routine diagnostic test. Unfortunately, the moment of onset of slurred speech is too indefinite to be used alone as the end-point, except in extreme cases. It is suggested that manifest anxiety probably reflects increased cerebral excitability.

J. L. Standen

476. **Improving Senile Behaviour with Reserpine and Ritalin. New Approach with Use of Methyl Phenylpiperidylacetate**

J. T. FERGUSON and W. H. FUNDERBURK. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 259–263, Jan. 28, 1956. 2 figs., 1 ref.

The effectiveness of " serpasil " (reserpine) and " ritalin " (methyl phenidate), given by mouth, in controlling abnormal behaviour manifestations was studied in 215 psychiatric patients aged 60 to 84 over a period of 11 months at Traverse City State Hospital, Michigan. The initial dosage was based on an evaluation of the individual patient in respect of 11 categories of behaviour, and at first methyl phenidate was given to 62 patients showing mainly negativism, reserpine to 131 showing mainly overactivity, and both drugs to the remaining 22.

The choice of drug and the dosage were subsequently adjusted in each case according to clinical progress and side-reactions. It was eventually found in most cases that more benefit was derived from both drugs given together than from either separately. After 4 to 8 months 67 patients were able to discontinue taking the drugs entirely, the remainder continuing to take maintenance doses.

The clinical results were most satisfactory and suggest that the drugs should be suitable for use in general practice. Of the 215 patients, 171 showed an improvement in behaviour, while the remaining 44 and a control group of geriatric patients showed little change. The effectiveness of the drugs was verified by the substitution of placebos in successful cases. No contraindications were found in respect of age, duration of illness, or abnormal physical findings. The primary effect of the drugs appeared to be a lessening of confusion and an improvement in orientation, as a result of which other forms of therapy might become possible. Although psychotherapy was not carried out in these patients, the authors consider that in view of the complex nature of their illnesses a single method of treatment is not sufficient in itself. Unless the patient was helped into a new situation, the improvement from the mental awakening produced by the drugs was minimal.

N. A. Standen

477. **Dangers in Combining Reserpine (Serpasil) with Electroconvulsive Therapy**

M. W. FOSTER and R. F. GAYLE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 1520–1522, Dec. 17, 1955. 6 refs.

Severe reactions, causing death in one instance, occurred in 6 out of 63 patients given electric convulsion therapy (E.C.T.) with reserpine at the Medical College of Virginia, Richmond. In the fatal case the patient had received reserpine by mouth for 3 days before admission to hospital; on admission he was given an intramuscular injection of 2·5 mg. of the drug. This injection was repeated on the morning of the third day, and 4½ hours later he was given E.C.T. Pulse and respiration ceased and stimulants had no effect. At necropsy no anatomical cause for death could be found. The second case was somewhat similar, but the patient responded to stimulants. In the third case a course of E.C.T. (to a total of 9 treatments) had been given before reserpine therapy started. After 2 injections, each of 2·5 mg., of reserpine one further administration of E.C.T. was followed by collapse, with apnoea and an almost imperceptible pulse. The patient responded gradually to stimulants. In the fourth case the patient was given E.C.T. while receiving 1 mg. of reserpine daily by mouth; the third administration of E.C.T. was followed by cessation of pulse and a prolonged period of apnoea. In 2 further cases in which both E.C.T. and reserpine were given there was a precipitous fall in blood pressure lasting several hours. All the patients remained drowsy, lethargic, or confused for several hours after resuscitation. No adequate or predictable cause for the collapse could be found, and there was no correlation between the amount or the route of administration of reserpine and the severity of the reaction.

The dose of E.C.T. applied in these cases was minimal.

E. H. Johnson

478. **A New Drug to Relieve Anxiety**

E. B. DAVIES. *British Medical Journal* [*Brit. med. J.*] **1**, 480–484, March 3, 1956. 9 refs.

Benactyzine hydrochloride ("suavitil"), an anticholinergic drug, is the hydrochloride of the diethylaminoethyl ester of benzilic acid and is claimed by Jacobsen (*Dan. med. Bull.*, 1955, **2**, 159) to relieve anxiety, especially in psychoneurotic patients. [See also *Abstracts of World Medicine*, 1956, **19**, 312.]

At Addenbroke's and Fulbourn Hospitals, Cambridge, the author used the drug in the treatment of 56 men and 54 women with various psychiatric disorders, 74 of them as out-patients. The dose varied from 1 to 4 mg. given by mouth up to 4 times daily. Side-effects observed included palpitation, dryness of the mouth, loss of concentration and a sensation of vagueness, and dizziness.

Improvement was noted in 2 out of 8 schizophrenics; in 11 of 14 depressives; one of 2 manic-depressives; one of 5 hysterics; 4 of 5 with obsessional states; 15 of 22 anxiety neurotics; 11 of 16 alcoholics; 10 of 21 cases of tension, anxiety, and depression; and in 12 of 14 cases of psychosomatic disorders of various types. Deterioration occurred in one case of hysteria, 2 of obsessional state, and 5 of tension, anxiety and depression. The remainder were unchanged. Males responded better than females. Analysis showed that the patients fell roughly into two groups: those who wished, consciously or unconsciously, to derive benefit did so providing definite anxiety was present; those who were hostile, overtly, hysterically, or by means of projection, failed to improve. These reactions are somewhat similar to those seen with barbiturates and other sedatives, but apparently they do not occur with chlorpromazine. Patients who derived benefit from benactyzine reported that they felt "calm" or "soothed". It is advised that the drug be used with discrimination. Frank hostility is a contraindication, while cases of psychosexual disorder should be treated cautiously, if at all. Cases of reactive depression failed to improve, but anxiety due to tension from the environment was relieved.

G. de M. Rudolf

479. **Group Behaviour in Chronic Schizophrenics Treated with "Meratran"**

F. HOUSTON. *British Medical Journal* [*Brit. med. J.*] **1**, 949–952, April 28, 1956. 14 refs.

The author reports from Fulbourn and Addenbrooke's Hospitals, Cambridge, that a carefully controlled study of the effect of "meratran" on 10 male chronic schizophrenic patients (10 similar patients receiving a placebo) showed that the drug was ineffective, though the patients improved on account of the increased attention they received and the raised morale among the nursing staff (who appreciated the fact that they were taking part in a programme of clinical research).

F. K. Taylor

Dermatology

480. **The Formaldehyde Treatment of Plantar Warts**
R. B. COLES. *Transactions of the St John's Hospital Dermatological Society* [*Trans. St. John's Hosp. Derm. Soc. (Lond.)*] 18–19, No. 35, 1955. 4 refs.

At the Northampton and Kettering General Hospitals during 1951, 229 patients with plantar warts were treated initially with 3% formaldehyde solution (formalin) in order to assess the value of this treatment. The method of application and the different types of case are described. The treatment was successful in 49·3% of cases in under 7 weeks, the remaining cases being then treated by other methods. In view of the results and the painlessness of the procedure (compared with solid carbon dioxide, for example) the author maintains that the formalin method still has a useful place in the treatment of plantar warts. *G. B. Mitchell-Heggs*

481. **Hydrocortisone (Compound F) Acetate Ointment in Dermatological Therapy**
B. PORTNOY. *Transactions of the St. John's Hospital Dermatological Society* [*Trans. St John's Hosp. derm. Soc. (Lond.)*] 14–17, No. 35, 1955. 23 refs.

After a brief review of some of the previously published reports concerning the topical application of hydrocortisone (Compound F) in the treatment of dermatological conditions the author presents, from the Manchester and Salford Hospital for Skin Diseases, the results obtained in a series of 226 cases treated with hydrocortisone ointment in concentrations of 1% or 2·5% in a lanolin and soft paraffin base. The various types of response in a variety of superficial inflammatory dermatoses are recorded in tabular form, while those in cases of pruritus ani, pruritus vulvae, and infantile eczema are described in more detail. In the former group a " particularly good " response was obtained in 74 cases and " a positive therapeutic effect " in a further 106. A tendency to relapse on cessation of treatment was noted. *G. B. Mitchell-Heggs*

482. **Topical Hydrocortisone Therapy in Diseases of the Skin: A Clinical Evaluation**
I. M. WARTZKI and B. R. ENTWISLE. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 318–326, Feb. 25, 1956. 2 refs.

The authors have analysed the results of treatment with local applications of hydrocortisone ointment in 100 cases of diseases of the skin seen in private practice in Melbourne. The conditions treated included dermatitis due to various causes, eczema of various sites, Besnier's prurigo, neurodermatitis, discoid eczema, otitis externa, pruritus ani et vulvae, genito-crural and gluteal intertrigo, and one case each of morphoea (localized scleroderma), purpuric eruption, Jacquet's napkin erythema, erythema due to DDT, and erythema multiforme of the lips. Brief notes of the results obtained are set out in a series of tables and a selection of cases from each type of dermatosis are described in greater detail.

On the whole the results were very satisfactory and the authors conclude that hydrocortisone ointment has a definite place in the treatment of skin disease, but warn against its indiscriminate use, since in unsuitable cases the result obtained may be inferior to that with other remedies. The best results were seen in erythema multiforme, papular urticaria (so often refractory to treatment), eczema, pruritus ani, and intertrigo; in the cases of Besnier's prurigo, discoid eczema, and otitis externa the results were disappointing. *G. B. Mitchell-Heggs*

DERMATOSES

483. **Nummular Eczema**
A. I. WEIDMAN and H. H. SAWICKY. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **73**, 58–65, Jan., 1956. 2 figs., 13 refs.

Nummular or discoid eczema is a common dermatosis characterized by the appearance on the skin of " discrete coin-shaped erythematosus [*sic*] plaques studded with small vesicles and papulovesicles ". After a brief review of some of the relevant literature, the authors analyse the records of 125 (out of a total of 516) patients treated during the last 8 years at the New York University Hospital who were subsequently re-examined.

The sex incidence was about equal; analysis of the patients' occupations showed a preponderance of housewives, manual workers and clerical workers being the next most frequently affected. Only 17 patients stated that they used soap and water to excess, but in most even their normal use aggravated the condition. Nummular eczema occurred most frequently in the younger and middle age groups, the maximum incidence being between 30 and 35 years, while its duration before consultation at the authors' clinic varied from a few days to 35 years. The dorsa of the hands and fingers and the extensor surfaces of the forearms were most commonly involved, the extensor aspects of the legs less so, and the trunk and face infrequently. The condition showed a seasonal variation in most cases, being worse in winter in 72, in spring or autumn in 5, after " nervous upset " in 3, and after each pregnancy in one. A history of hay-fever, asthma, or atopic eczema was given by 14 patients, and 20 stated that at least one of these conditions was present in members of their immediate family. A positive reaction to patch-testing with potassium bromide was obtained in 75, and with potassium iodide in 78, out of 104 cases so tested, whereas corresponding tests in 100 cases with dermatoses other than nummular eczema gave a positive reaction in 26 to the former and in 47 to the latter agent.

Topical application of iodochlorhydroxyquin (vioform) or the tars resulted in the most satisfactory response. Hydrocortisone applied locally, alone or combined with antibiotics, was efficacious in the more recently treated cases, but these results are not evaluated in this report.

The authors suggest that nummular eczema " may not be a disease entity at all, but rather a symptom complex caused by multiple etiologic factors, many of which remain obscure ". *Benjamin Schwartz*

484. **A Clinical Evaluation of Prednisone in the Treatment of Dermatoses**
C. R. REIN and E. I. BODIAN. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **73**, 378–381, April, 1956.

485. **Lichen Planus Treated with ACTH**
R. H. MEARA. *Transactions of the St. John's Hospital Dermatological Society* [*Trans. St John's Hosp. derm. Soc. (Lond.)*] No. 34, 17–19, 1955. 3 refs.

Following the dramatic cure of one case of severe acute lichen planus in 1953 with ACTH (corticotrophin) administered in a slow intravenous infusion, a further 10 such patients have now been treated at St. John's Hospital for Diseases of the Skin, London, in the same way. The type of lesion treated, the dosage used, and the side-effects noted (chiefly gain in weight) are described.

In all cases the symptoms were controlled within a few days and the eruption resolved within 14 to 28 days. Relapse occurred in one case before the end of treatment and in another 2 cases within one to 2 months of stopping treatment. The hormone had to be withdrawn in one case in which the patient developed oedema and mental changes. The author suggests that there is probably a place for ACTH in the treatment of cases of widespread lichen planus which is causing distressing and disabling symptoms. *G. B. Mitchell-Heggs*

486. **Mepacrine in Rosacea.** [In English]
P. M. INMAN and B. GORDON. *Acta dermato-venereologica* [*Acta derm.-venereol. (Stockh.)*] **35**, 446–452, 1955. 5 refs.

The authors briefly summarize the literature on the aetiology of rosacea. Capillary damage due to light being, in their opinion, a major factor, it seemed likely that mepacrine might act by decreasing the sensitivity of the skin to light. At the Sunderland and West Hartlepool Skin Clinic, therefore, 50 patients with rosacea uncomplicated by keratitis were divided into two equal groups at random, one being treated with *x* rays (two doses of 70 r at 2 weeks' interval) and the nightly use of a sulphur and salicylic acid ointment as a control group, and the other with 300 mg. of mepacrine daily. The results in both groups were assessed objectively and subjectively at the end of 4 weeks.

Of the control group, 15 (60%) showed great subjective and objective improvement and only 4 (16%) showed no significant improvement. Of the patients treated with mepacrine, 6 (24%) showed great objective improvement and 11 (44%) claimed great subjective improvement, while in 6 (24%) there was no objective or subjective improvement. There was no sex difference in the response to either form of treatment. In spite of a uniform dosage of mepacrine the degree of discoloration of the skin varied greatly between patients. In 8 cases mepacrine treatment was continued and produced progressive improvement, much beyond that found at the end of the 4-week period. *F. Hillman*

487. **Antimalarials in the Treatment of Discoid Lupus Erythematosus. Special Reference to Amodiaquin (Camoquin)**
R. W. LEEPER and M. F. ALLENDE. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **73**, 50–57, Jan., 1956. 24 refs.

This paper from the University of California School of Medicine, San Francisco, reports a comparative study of 3 antimalarial drugs—" quinacrine " (mepacrine), chloroquine, and amodiaquin (camoquin)—in the treatment of a recent series of 32 cases of discoid lupus erythematosus.

Mepacrine was given in a dosage of 0·3 g. daily initially, reduced to 0·2 g. daily when skin discoloration appeared, and maintained at 0·1 g. daily for prolonged treatment. Of 16 patients treated with this drug, 5 improved sufficiently for treatment to be stopped after 3 months (but all had to be re-treated within an average of 3 months), 10 showed " encouraging " improvement at first but this was not maintained, and one developed sensitivity to the drug.

Of 29 patients who received one or more courses of chloroquine, starting with 0·5 g. daily for 2 weeks and continuing with 0·25 to 0·5 g. daily, in 22 the condition improved or cleared up entirely (12 relapsed within one year), in 5 the rate of improvement was so slow that other measures had to be adopted, the treatment of one was abandoned because of enteritis, and one declined further treatment because of early aggravation of the lesions.

Amodiaquin was given to 16 patients, most of them receiving 0·2 g. daily; 8 of these had previously received both mepacrine and chloroquine, and 6 chloroquine only. Remission occurred in 9 cases although in one this lasted only a month, and considerable improvement was reported in the remainder after 6 months' follow-up. Skin pigmentation did not occur, nor were gastro-enteritis, dyspepsia, blurring of vision, or drug sensitivity reported in any case even where these had occurred during treatment with chloroquine or mepacrine. The commonest side-effect was a feeling of fatigue and lassitude, and only when the daily dose was increased to 0·4 g. did vertigo, weakness, and malaise occur. Tolerance to amodiaquin in general was good, even after 8 months' treatment in one case.

These antimalarial drugs appear to be more effective and safer than treatments previously used in the control of discoid lupus erythematosus. The authors' limited experience with amodiaquin suggests it is similar to chloroquine in effect and that either of these drugs is preferable to mepacrine. *Benjamin Schwartz*

Paediatrics

488. **The Incidence of Milk Allergy in Pediatric Practice**
C. COLLINS-WILLIAMS. *Journal of Pediatrics* [*J. Pediat.*] 48, 39–47, Jan., 1956. 18 refs.

The author has reviewed the clinical histories of 3,000 infants and children seen by him in private paediatric practice in Toronto in order to ascertain the incidence of milk allergy. As those known or thought to be suffering from major allergies were excluded the incidence in this series is lower than that generally reported, only 9 infants (an incidence of 0·3%) being found to be allergic to milk. The cases of these infants are reported individually.

The diagnosis was made on clinical grounds and on therapeutic evidence that omission of milk from the diet caused complete remission of the symptoms. In 7 cases the symptoms were intestinal, manifested by vomiting, diarrhoea, and colic, while one infant presented with a behaviour disorder and one with anaphylactic shock. The author emphasizes that although the incidence of this type of allergy is low, its diagnosis and treatment are nevertheless worth while since they usually result in complete relief of symptoms that might otherwise prove baffling and resistant to the usual measures. He points out that, contrary to the finding of other workers, the series included no case in which colic was the only symptom. *David Morris*

NEONATAL DISORDERS

489. **The Nature of the Hyaline Membranes in Asphyxia of the Newborn**
D. GITLIN and J. M. CRAIG. *Pediatrics* [*Pediatrics*] 17, 64–71, Jan., 1956. 19 figs., 20 refs.

This paper from the Harvard Medical School reports the results of a painstaking biochemical investigation into the nature of pulmonary hyaline membrane. The usual histochemical techniques were employed and, in addition, the membranes were studied by fluorescent antibody and dye-staining procedures. The antisera used had been prepared and rendered specific against human fibrin, plasma albumin, gamma globulin, and β_1-metal-combining globulin. Human amniotic fluid was also examined by the same techniques.

It was shown that hyaline membrane was composed mainly of fibrin, and that only relatively small amounts of fibrin were found in the amniotic fluid. The authors conclude that a hyaline membrane may result from effusion from the pulmonary circulation, followed by conversion of the fibrinogen to fibrin and thence syneresis of the fibrin to form a membrane. They acknowledge that membranes so formed are not entirely composed of fibrin but also contain other elements such as squames from the amniotic fluid. They suggest, however, that the low fibrin content of the amniotic fluid argues against the formation of hyaline membrane as a result of inspissation of aspirated amniotic fluid. *I. A. B. Cathie*

490. **Neonatal Meningitis. Investigations of Sources and Routes of Infection**
A. DUPONT and E. THAMDRUP. *Danish Medical Bulletin* [*Dan. med. Bull.*] 3, 6–14, Feb., 1956. 1 fig., 43 refs.

The diagnosis, clinical features, and treatment of meningitis in the newborn are reviewed with reference to 9 cases seen at the Children's Hospital, Martinsvej, Denmark, in which infection was due to *Escherichia coli*. Of the 9 infants, 5 died; hydrocephalus developed in 2 of the survivors and the remaining 2 recovered completely. In 6 cases culture of specimens of blood and of nasal and faucial swabs yielded *E. coli* of the same subtype as that found in the cerebrospinal fluid; in one of these cases there was also otitis media due to *E. coli*. Two of the mothers harboured the organisms—in the vagina and in the urine and faeces respectively.

The authors conclude that the portal of entry is the upper respiratory tract or, in some cases, the umbilicus. They state that the investigation did not reveal any evidence that certain groups or subtypes of *E. coli* are of special aetiological importance in neonatal meningitis. *Winston Turner*

491. **The Failure of Hydrocortisone to Affect Neonatal Jaundice**
J. F. DESFORGES and T. O. VILLADOLID. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **91**, 126–130, Feb., 1956. 3 figs., 13 refs.

492. **Fetal Hemoglobin in Postmature Newborn Infants**
A. ABRAHAMOV, M. SALZBERGER, and Y. M. BROMBERG. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **26**, 146–150, Feb., 1956. 1 fig., 13 refs.

Foetal haemoglobin constitutes about 90% of the total haemoglobin content of the blood up to the 36th week of pregnancy, and an average of 80% at birth. After this the proportion decreases gradually, being about 70% at 2 weeks and 50% at 4 weeks of age. The outstanding feature of foetal haemoglobin is that its affinity for oxygen is greater than that of adult haemoglobin, a property which is important in view of the low oxygen tension in the placenta. The frequent incidence of anoxia in postmature newborn infants might therefore be the result of a reduction in the proportion of foetal haemoglobin present, and this hypothesis is supported by the finding by the present authors of an average of 65·1% (range 54·4 to 76·4%) of foetal haemoglobin in the blood of 17 postmature infants at birth, compared with an average of 85·5% in that of 100 normal full-term

infants examined at Hadassah University Hospital, Jerusalem. Thus the presence of a diminished concentration of foetal haemoglobin in the infant's blood may be of value in the postnatal diagnosis of postmaturity. *H. Lehmann*

CLINICAL PAEDIATRICS

493. **The Normal P–R Interval in Infants and Children**
M. M. ALIMURUNG and B. F. MASSELL. *Circulation* [*Circulation (N.Y.)*] **13**, 257–262, Feb., 1956. 3 figs., 34 refs.

Since changes in the length of the P–R interval " are of significant clinical value " in the study of rheumatic myocarditis, it is essential to know what variations are to be found in the length of this interval in normal infants and children. At the Children's Medical Center (Harvard Medical School), Boston, the P–R interval (or the P–Q interval when a Q wave could be detected) was measured in Lead II of the electrocardiogram of 506 healthy children. For special accuracy the tracing was magnified approximately 10 times by means of a reflectoscope when the measurements were being made. An analysis of the results showed that the child's age influences the length of the P–R interval; its mean duration was 0·114 second at the age of one year and 0·15 second at the age of 13. Moreover, with increasing heart rate the P–R interval becomes shorter, the mean value being 0·146 second at a heart rate of 65 per minute and 0·103 second at a heart rate of 185 per minute.

The average duration of the P–R interval in the 26 newborn babies in the present series ranged from 0·103 second at a heart rate of 91 to 110 per minute to 0·098 second at rates above 150 per minute. For infants of 1 to 9 months (63) the corresponding values were 0·120 second and 0·100 second. For children of 3 to 5 years (122) the average P–R interval was 0·129 second at heart rates of 71 to 90 per minute and 0·116 second at 131 to 150 per minute. And for children of 6 to 13 years (197) the figure was 0·142 second at rates below 71 per minute and 0·134 second at 111 to 130 per minute.
H. E. Holling

494. **Hypertonic Dehydration in Infancy**
W. B. WEIL and W. M. WALLACE. *Pediatrics* [*Pediatrics*] 17, 171–183, Feb., 1956. 2 figs., 48 refs.

Loss of body fluid is often accompanied by loss of electrolyte in a proportion equivalent to its concentration in the body fluids, but in certain circumstances an excessive water loss may occur and increased osmolarity of body fluids (hypertonicity) result. During a 15-month period beginning in January, 1953, 26 infants with hypertonic dehydration were studied at the Babies and Children's Hospital (Western Reserve University), Cleveland, this group including all infants with a concentration of sodium in the serum of 160 mEq. per litre or more. The primary condition responsible for the dehydration in 20 of the 26 infants was gastro-enteritis; unlike the anxious, shock-like appearance characteristic of salt depletion, these patients presented signs of depression of the central nervous system varying from lethargy to coma. Increased muscular tone was present, the tendon reflexes were exaggerated, convulsions were frequent, the cerebrospinal fluid showed an increased protein content, and abnormalities appeared in the electroencephalographic recordings. The urine was of low specific gravity despite the dehydration, the sodium and chloride content was low, urea clearance was less than 10% of normal, and the blood urea nitrogen level was high.

Complete balance studies, carried out on 5 patients, showed water loss in excess of sodium loss, no significant change in potassium balance (probably because of renal incompetence), a markedly positive chloride balance, and elevation of the serum chloride concentration. The chloride space remained relatively unchanged from normal during the illness and the recovery phase, the loss of water being almost entirely from the intracellular fluid compartment. The importance of treatment with fluids poor in electrolytes (sodium 50 to 60 mEq. per litre and chloride 35 to 45 mEq. per litre) is stressed, and rehydration at a slow rate—about 180 ml. per kg. body weight per 24 hours—is advised so as to avoid serious convulsive disturbances resulting from water intoxication. *R. M. Todd*

495. **An Epidemic of Acute Bronchiolitis in Infancy**
J. B. HEYCOCK and T. C. NOBLE. *British Medical Journal* [*Brit. med. J.*] **1**, 438–439, Feb. 25, 1956.

The authors describe an epidemic of acute bronchiolitis which occurred in infants during the months of October, November, and December, 1953, observations being made on 164 such cases in children under 2 years of age admitted to the Children's Hospital, Sunderland, during that period. Generally, 2 to 4 days after a simple upper respiratory tract infection, the child's condition deteriorated suddenly and rapidly, with distressing cough, wheezing, cyanosis, frothing at the mouth, and in some cases collapse. Clinical examination showed tachycardia and rhonchi and crepitations over both lungs, this picture being maintained for 3 or 4 days until, usually quite suddenly, the child seemed better, although the bronchospasm generally took longer to clear. Examination of the blood serum from a small number of cases showed no rise in titre of antibodies to the viruses of influenza or psittacosis, or to *Streptococcus* MG. The mortality rate was 6% (10 deaths, all in infants under one year of age) and relapse after apparent recovery occurred in 2·5%.

Treatment was arbitrary and to some extent standardized. Oxygen, intramuscular penicillin, and chlortetracycline (aureomycin) were given in all cases, and most of the patients were discharged from hospital within 2 weeks. The absence of significant pyogenic organisms from cultures of the sputum, combined with the appearance of the lungs at necropsy, suggested that the infecting organism was a virus. The authors consider that the disease is more common than published reports would indicate; it is appreciated that acute bronchiolitis is not distinguishable from bronchopneumonia in young babies. Follow-up studies revealed

no residual pulmonary complications. The notable features of this illness are its extremely rapid development, especially as the rise of temperature may be small, and the equally rapid recovery once the crisis has passed. The great value of oxygen in treatment is emphasized.

J. M. Smellie

496. Interstitial Plasma Cell Pneumonia

W. L. DONOHUE. *Laboratory Investigation* [*Lab. Invest.*] 5, 97–105, Jan.–Feb., 1956. 6 figs., 15 refs.

The author describes the post-mortem findings in 2 full-term infants who died at the Hospital for Sick Children, Toronto, after illnesses lasting 6 weeks in one case and more than a year in the other. The main clinical features were a moderate pyrexia, cyanosis, and respiratory distress. At necropsy in both cases the lungs were found to be bulky, firm in consistency, and rubbery. Histological examination showed a massive infiltration of the pulmonary interstitium with monocytes, lymphocytes, and a fair number of plasma cells. The air spaces contained foam cells, but no " honeycomb " material; *Pneumocystis carinii* was not demonstrable. The alveoli were lined by modified cuboid epithelium. A conspicuous finding was a thick, eosinophilic membrane lining many of the air spaces.

[The findings show clearly that this type of interstitial pneumonia differs from that caused by *Pneumocystis carinii*. The plasma cells, which may be scanty or absent in the latter disease, are obviously a non-specific phenomenon. Although the presence of fibroblasts is not specially mentioned in the description of the histological findings, the pulmonary changes in these two cases are reminiscent of those described by Hamman and Rich in adults under the name of " acute diffuse interstitial fibrosis of the lungs " (*Bull. Johns Hopk. Hosp.*, 1944, 74, 177).] *H. S. Baar*

497. Hyperthyroidism in Children: Observations in 50 Treated Cases, Including an Evaluation of Endocrine Factors

J. C. MCCLINTOCK, T. F. FRAWLEY, and J. H. P. HOLDEN. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] 16, 62–85, Jan., 1956. 3 figs., 43 refs.

At Albany Hospital, Albany, New York, 50 cases of hyperthyroidism in children aged 2 to 15 years, 48 of whom were female and 2 male, were treated between 1918 and 1955. Some form of surgery, most frequently one-stage bilateral total thyroidectomy, was employed in 45 cases, 30 of which were treated before the antithyroid drugs became available; of the 20 patients diagnosed since their advent, 19 were treated with these drugs. At the time of diagnosis 26 patients had bilateral exophthalmos, and 22 of these underwent thyroidectomy, with no improvement in 6 cases and postoperative progression of the exophthalmos in one.

The symptoms of hyperthyroidism in children are similar to those in adults, but there are certain specific differences, particularly in respect of disturbances of the central nervous system, which account for most of the symptoms in the former whereas cardiovascular disturbances predominate in the latter. In the present series 52% of the patients were brought to the physician on account of an enlarged thyroid gland. Apart from tachycardia, cardiovascular signs were less frequently found than in adults. Increased linear growth was observed in 14% of cases, but it was found that the acceleration in growth and development occurred only after hyperthyroidism had been present for some time—probably at least 6 months. It has been suggested that acceleration of growth, when it occurs, is due to an element of hyperpituitarism as an aetiological factor in juvenile thyrotoxicosis, whereas the delay in maturation of secondary sex characteristics which has occasionally been reported in this condition would indicate an element of hypopituitarism. In the present series there was no evidence of any significant effect on the age of onset of menstruation or on the menstrual pattern when established. In fact, it was infrequent for there to be any evidence of endocrine changes either as precursors or as sequelae of the thyrotoxicosis, and the authors consider that " previous concern about possible disturbances in growth, alterations in menses and fertility, and other endocrine disturbances, appears to have been overemphasized ".

Thyroidectomy after suitable preparation resulted consistently in rapid and permanent control of the thyrotoxicosis, and complications were rare. Growth disturbances were uncommon after thyroidectomy and appear to be less likely to occur than was once believed, provided care is exercised in maintaining a normal thyroid state after the operation. Antithyroid drugs, when used in the treatment of juvenile thyrotoxicosis, should be given in full adult dosage and continued long enough to restore a euthyroid state and to maintain it for 12 to 18 months. This may secure permanent relief from symptoms and regression of the goitre, but the authors consider that surgical resection of the thyroid gland after proper preparation with antithyroid drugs remains the most satisfactory form of treatment.

John Lister

498. The Treatment of Hyperthyroidism in Childhood with Thiouracil Drugs.

J. J. VAN WYK, M. M. GRUMBACH, T. H. SHEPARD, and L. WILKINS. *Pediatrics* [*Pediatrics*] 17, 221–229, Feb., 1956. 2 figs., 18 refs.

During the past 10 years all children with hyperthyroidism at the Harriet Lane Home (Johns Hopkins University), Baltimore, have been treated medically with antithyroid drugs, and in this report the authors review the results in 16 in whom the condition developed between the ages of 4 and nearly 13 years. Initially propylthiouracil was given daily in a dosage of 300 mg. for a period of 3 weeks, after which the dose was adjusted to the needs of the individual child. Of 8 children who were treated for periods of 1 to 5 years, all have remained in remission after discontinuing the drug, even though 7 of them have passed through puberty and adolescence. In 4 cases surgical treatment became necessary, in one because of drug rash and in 3 because of failure to carry out adequate medical treatment; one of these patients died postoperatively in thyroid crisis, and 3 became

hypothyroid and now need thyroid therapy. The remaining 4 children are still under treatment, one after a period of 7 years; in the other 3 the thyroid gland showed progressive enlargement, but under treatment with thyroid extract in addition to propylthiouracil the thyroid enlargement has disappeared.

The authors consider that drug therapy is the treatment of choice for young patients and that surgery should be reserved for patients who develop drug sensitivity or fail to cooperate. They suggest that antithyroid treatment should be continued until there is substantial reduction in the size of the gland, that is, usually for at least 2 years. *R. M. Todd*

499. **The Pattern of the Electrolyte Excretion in the Urine of Babies Born to Diabetic Mothers**
T. STAPLETON. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 42–43, Feb., 1956. 3 figs., 5 refs.

The urinary excretion of electrolytes in 5 babies born to diabetic mothers was studied at St. Mary's Hospital, London. In order to eliminate variations due to such factors as gestational age, oedema, and birth by Caesarean section, the excretion in mEq. per kg. at the lowest weight reached during the first three days of life was taken as the standard for comparison. On this basis no abnormality was detected in the urinary excretion of sodium, potassium, or chloride, any variation between the infants being accounted for by differences in gestational age.
I. Ansell

500. **Epilepsy and Cerebral Palsy**
B. H. KIRMAN. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 1–7, Feb., 1956. 2 figs., 11 refs.

The author discusses the double handicap of cerebral palsy and epilepsy in children, in relation to the possible educability of such patients. Reviewing the incidence of the association of the two lesions he reports that a study carried out at the Fountain Hospital, London—which cares mainly for children certified as mentally defective—showed that the incidence of epilepsy among 228 children with cerebral palsy (of whom nearly half had spastic diplegia) was 45% (103 cases). Of the 138 patients with spastic diplegia and hemiplegia, 69 (50%) had epileptic fits, compared with only 4 (26%) out of the 19 with athetosis. Fits never occurred in patients with "pure" athetosis or in cases of ataxia with lack of muscular coordination in which the muscle tone was low. The frequency of fits at first increased, but tended to fall with the approach of puberty.

Fully developed major convulsions were rare, the manifestations consisting variously in attacks of pallor, dreaminess, screaming fits, isolated myoclonic jerkings, and unexplained falls. Intelligence tests—which in such cases must be regarded as of only limited significance—suggested that patients with cerebral palsy complicated by epilepsy were likely to be less intelligent on the average than those without this complication. Electroencephalographic recordings showing phenomena of an "epileptic" type were also obtained in patients in whom no fits had been observed in hospital. The post-mortem findings in 16 cases of cerebral palsy revealed that in all of them there was reduction in the size of the brain, with diffuse gliosis involving the cerebral cortex and often other structures. The author found no evidence in this series to support the thesis of subcortical epileptic foci. *I. Ansell*

501. **Thrombocytopenic Purpura and Chickenpox**
R. G. WELCH. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 38–41, Feb., 1956. 37 refs.

The author reports the occurrence of acute thrombocytopenic purpura following chickenpox in 3 cases seen at St. Thomas's Hospital, London. The patients, all of whom were female, were aged 6 years, 26 years, and 19 months, and the haemorrhagic symptoms developed 1 week, 2 weeks, and 4 to 5 weeks respectively after the onset of chickenpox; they were transient in all 3 patients, but in the first continued for 10 weeks. The third patient, aged 19 months, had a large haemangioma covering the left pectoral area, and the author discusses the possibility of a causal relationship between this and the thrombocytopenia.

Reference to the literature shows that many viral or bacterial infections, particularly in childhood, may be followed by thrombocytopenia, and the theory that this is caused by an allergic response to the infecting organism is supported by the occurrence of an interval between the onset of the preceding illness and the start of purpuric symptoms; this varies from a few days to 4 or 5 weeks, but most commonly it is about one week. There is no relationship between the severity of the preceding illness and the occurrence or severity of subsequent thrombocytopenia. *A. S. Douglas*

502. **Electro-encephalography in Children with Recurrent Abdominal Pain**
J. APLEY, J. K. LLOYD, and C. TURTON. *Lancet* [*Lancet*] **1**, 264–265, Feb. 11, 1956. 16 refs.

A controlled electroencephalographic study was made of 133 children who had a history of recurrent abdominal pain of at least 3 months' duration and in whom no evidence of organic disease was found. The children were between 3 and 14 years of age, 96 of them having been referred to a hospital out-patient department and 37 being obtained from among children attending school clinics for routine examination. Any who had fits in addition to the abdominal pain were excluded from the survey. An equal number of children of approximately the same ages, but who had no abdominal pain or fits, were studied as controls. No significant differences were found between the hospital patients and the school-children.

The incidence of electroencephalographic abnormalities of all types was very similar in both groups, "epileptic" features being found in 14 cases in each.

The authors consider that abdominal pain as a sole manifestation of epilepsy must be rare, and even the overt association of pain with fits is relatively unusual. They consider that "children with no symptoms other than recurrent abdominal pains should no more be considered 'epileptic' than children without them".
John Lorber

Public Health and Industrial Medicine

503. **Evaluation of Poliomyelitis Vaccination in Massachusetts**

A. S. POPE, R. F. FEEMSTER, D. E. ROSENGARD, F. R. B. HOPKINS, B. VANADZIN, and E. W. PATTISON. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 110–117, Jan. 19, 1956. 3 figs., 1 ref.

The State of Massachusetts experienced the largest epidemic of poliomyelitis in its history during the summer of 1955, a few months after immunization of approximately one-third of the children in the State aged 6 to 10 years with one or more doses of Salk-type poliomyelitis vaccine. In addition, a few children had received a full course of 3 doses of vaccine the year previously and some of these had had a booster dose in 1955. Once it became clear from the rapid increase in the incidence of the disease during the first week in July that an epidemic was in progress, the Massachusetts Department of Health undertook a special investigation into the protective effect of the vaccination. Most of the cases occurring were due to Type-1 virus.

The total population at risk in the age groups concerned was 439,097, of whom 278,532 had received no vaccine. There occurred 553 cases of poliomyelitis (paralytic and non-paralytic) amongst the unvaccinated children—an attack rate of 198·2 per 100,000—whereas among 137,968 children who had received only one dose of vaccine (76 of them in 1954) there were 130 cases—an attack rate of 94·5 per 100,000. Among 22,597 children who had been given two or more doses of vaccine there were 15 cases—an attack rate of 66·4 per 100,000. The effectiveness of a single dose of the vaccine in preventing Type-1 poliomyelitis in this epidemic is estimated as 53% for all cases and as 60% for paralytic cases. Owing to the small number of cases, the effectiveness of 2 or more doses could not be estimated accurately.

J. E. M. Whitehead

504. **The Influence of Acute Infectious Diseases on Immunity against Diphtheria in Immunized Children Given One Booster Dose.** (К вопросу о влиянии острых инфекционных заболеваний на иммунитет к дифтерии у однократно ревакцинированных детей)

A. G. STAROVEROVA. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 52–57, No. 2, Feb., 1956. 4 refs.

An analysis was made at the Institute of Epidemiology, Moscow, of Schick-test results in 4,183 children who had been immunized with diphtheria toxoid in infancy and had received a booster dose. In all, 15·6% of these children proved to be Schick positive; but among the children who had not suffered from other acute infectious diseases the proportion was significantly lower—5·2%—than among those who had suffered from one or more infectious diseases, the figure increasing from 12% among those who had had one or 2 infections (1,321 children) to 24% among those who had had 4 to 6 (761 children) and to 42·7% among those who had had 7 or more infections (269 children). These findings can be explained in part by the fact that the longer the period that had elapsed since the booster dose (and the lower the level of diphtheria antitoxin circulating in the blood), the greater had been the chance of contracting other diseases. This interval was a year or more in only 25·1% of those without a history of infectious diseases, 37·3% of those who had had one or 2, 45·1% of those who had had 3, and 56·6% of those who had had 4 or more infectious diseases.

On the other hand when acute infections occurring before the booster dose were considered, a higher proportion (3 to 5%) of positive reactors was found among those children who had one or more infections within 2 months of the booster dose than among those in whom infections occurred in the more distant past. Further support for the hypothesis that infections may lead to a reduction of specific antibody titres was obtained in a group of children who had suffered from infectious diseases after receiving the booster dose, the proportion of positive reactors being 8 to 14% higher among those whose infections occurred within 2 months than among those who had similar infections 6 to 11 months later.

K. Zinnemann

505. **Mortality from Fog in London, January, 1956**

W. P. D. LOGAN. *British Medical Journal* [*Brit. med. J.*] 1, 722–725, March 31, 1956. 2 figs., 5 refs.

Fog occurred in the London area on January 3, 1956, becoming thick on January 4 and persisting until January 6. In this paper from the General Register Office the numbers of deaths registered in Greater London during the weeks ending January 7 and January 14 are compared with those registered during the weeks ending December 24 and December 31, 1955, the figures indicating that an excess mortality of about 1,000 occurred during and immediately after the period of fog. The percentage excess of actual over expected deaths was greatest for infants under one, but in terms of actual numbers those over 65 were most affected. The greatest increase (123%) over the preceding period occurred in the number of deaths from bronchitis, and in this category the increase was again greatest over the age of 65 (161%). Deaths from pneumonia showed a 16% increase, from influenza 33%, from myocardial degeneration 24%, and from coronary arterial disease 17%. During the same two weeks the claims for sickness benefit in the Administrative County of London (the central part of Greater London) and in Middlesex increased by 72% compared with an increase of 41% in the remainder of England and Wales.

It is noteworthy that during this "smog" episode there was no large fall in mean daily air temperature, which at no time fell below freezing point. It does not

appear, therefore, that the excess mortality could be attributed to a very low air temperature. Air pollution with solid particles, measured at Kew with an Owen's smoke filter, apparently increased 4- to 5-fold, reaching a maximum on January 5 of 1·229 mg. per cu. metre.

Fog in December, 1952, was responsible for 4,000 deaths. As the author states, "these further 1,000 deaths last January are a stern reminder that this major public health problem has not yet been solved".

John Pemberton

INDUSTRIAL MEDICINE

506. **Antipruitic Protective Cream Containing Succinic Dinitrile in the Prevention of Occupational Dermatoses.** (La crème protectrice antiprurigineuse au dinitrile succinique dans la prévention des dermatoses professionnelles)

L. BORY and M. VALENTIN. *Archives des maladies professionnelles, de médecine du travail et de sécurité sociale* [*Arch. Mal. prof.*] **17**, 37–44, Jan.–Feb., 1956. 6 refs.

The antipruritic action of succinic dinitrile was noted by the senior author in 1950, when a preliminary study of its possible use as an ingredient of barrier creams for the prevention and cure of occupational dermatoses was carried out. This proved highly successful and a further clinical trial appeared justified, the results of which are now reported. A precise course of treatment and system of observation were formulated and applied to 16 persons —one a housewife—suffering from various forms of occupational dermatitis. In 13 of the cases the treatment was successful, complete cure being claimed in 9 cases within a period of one to 2 weeks. Only in 2 cases of eczema of long standing in uncooperative patients was the treatment without effect.

The conclusion is reached that treatment with a vanishing cream incorporating 3% of succinic dinitrile is highly efficacious in the treatment of occupational dermatoses and has the advantage that it does not call for any change in the working conditions or the nature of the patients' employment.

A. Meiklejohn

507. **The Pathogenesis of Silicosis. Solubility plus Foreign-body Reaction.** (Zur Pathogenese der Silikose. Löslichkeit plus Fremdkörperwirkung)

E. SCHILLER. *Archiv für Gewerbepathologie und Gewerbehygiene* [*Arch. Gewerbepath. Gewerbehyg.*] **14**, 1–9, 1955. 6 figs., bibliography.

This paper gives a brief report of experiments carried out on mice to investigate the combined effects on the tissues of insoluble diamond dust and a finely divided powder of the freely soluble silicic acid. The dusts were injected intraperitoneally and the surviving animals were killed on the 30th or the 60th day of the experiment. There were 4 groups, each of 10 mice, which received: (1) a single injection of 10 mg. of diamond dust of particle size 1 to 2 μ suspended in normal saline; (2) a single injection of 10 mg. of dried, pulverized silicic acid of particle size 200 Å. in normal saline, together with 10 μg. of cortisone on each of the first 3 days; (3) daily injections of 1 mg. of silicic acid in distilled water; and (4) diamond dust as in Group 1, but suspended in distilled water, and daily injections of 1 mg. of silicic acid as in Group 3.

In Group 1 9 mice survived 30 days and 8 survived 60 days. The diamond dust was found stored in the tissue cells, with slight fibrosis and an infiltration of lymphocytes. Those particles carried to the lymph nodes were stored in the central sinuses, where they were to be seen after 30 days. At 60 days a reticular network had appeared in the medulla and cortex of the lymph nodes. In Group 2, in spite of the administration of cortisone, only one mouse lived to the 30th day and was killed on the 35th. Giant-celled granulomata were found, with a network of young connective tissue, the histology resembling that of Boeck's sarcoid rather than that of a silicotic nodule. In Group 3 there were no early deaths, but all the animals died during the 3rd week. The adrenal glands showed no specific changes, but there were parenchymatous cysts in some organs, particularly in the liver. No fibrotic nodules were seen. From the findings in Group 4 it seemed probable that the diamond dust had adsorbed the silicic acid and so limited its toxicity. There was marked transference of the particles to the lymph nodes and to the liver. After 60 days primary granulomata were found, consisting of fibrous nodules with a hard core.

These findings are held to confirm the importance, in the development of nodular fibrosis, of the concurrence of the chemical irritant effect of soluble silicic acid and the mechanical effect of a foreign body.

M. A. Dobbin Crawford

508. **A New Viewpoint on Carcinoma of the Lung in Asbestos Workers.** (Neue Gesichtspunkte über den Lungenkrebs der Asbestarbeiter)

H. BOHLIG and G. JACOB. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **81**, 231–233, Feb. 17, 1956. 2 figs., 15 refs.

On the basis of their experience at the Dresden Municipal Hospital the authors discuss the development of cancer of the lung in workers in the asbestos industry, of which Dresden is an important centre.

Although lung cancer is commonly supposed to be the most frequent complication of asbestosis, male asbestos workers do not in fact appear to develop the disease more often than the population of Germany as a whole. However, the disease is more frequent in women asbestos workers, and tends to develop at a younger age than outside the industry. Moreover, in asbestosis the lower lobe is affected by cancer approximately 3 times more often than the upper, whereas usually the upper lobe is attacked twice as frequently as the lower. If asbestosis is present the prognosis and course of cancer of the lung are rather worse, as resection is often contraindicated by fibrosis and cor pulmonale.

The authors discuss the pathogenesis of cancer associated with asbestosis, and point out that such findings as the difference in sex incidence show that mechanical irritation by asbestos crystals cannot be the only factor involved. They recommend a review of all cases of carcinoma occurring in the asbestos industry as a whole

as a step towards clearing up some of the doubtful points. [The difference in sex incidence, if confirmed, would be of great importance. It is unfortunate, therefore, that more precise statistical information is not provided.]

W. K. Dunscombe

509. **The Effect of Vibration on Drivers of Heavy Self-propelled Machinery.** (Action des trépidations sur les conducteurs d'engins automobiles lourds)

V. RAYMOND. *Archives des maladies professionnelles, de médecine du travail et de sécurité sociale* [*Arch. Mal. prof.*] 17, 5–18, Jan.–Feb., 1956. 5 refs.

The adverse effects of vibration from machines or percussion tools on the workmen who operate them are well recognized, and vary with the frequency, rhythm, and amplitude of the vibrations. The present communication is restricted to a study of the effects of vibration on the drivers of heavy vehicles such as tractors, scrapers, bulldozers, and dumpers. A summary of the observations reported by various authors is given, from which it emerges that only a proportion of drivers are adversely affected. The complaints attributed to this cause include such general conditions as loss of appetite, loss of weight, headaches, and occasionally vertigo. Digestive disturbances are prominent, with abdominal pain, nausea, and occasionally vomiting, but there is no evidence of organic disease. Lumbar and other muscular pains also occur, again without evidence of an organic lesion. The effects appear after 6 to 8 months' work and are influenced by the unevenness of the ground, the speed of the vehicle, and the transmission to the driver of the jolting suffered by the frame of the machine. Drivers who already suffer from digestive troubles, lumbar and abdominal muscle weakness, and nervousness are particularly prone to react adversely. Alcoholism is an aggravating factor.

Prevention of the effects may be achieved by attention to the machines and the drivers. In the case of the machines attention should be directed to the provision of shock absorbers, improvement in the suspension of the driver's seat, and limitation of the speed of the vehicle. Drivers with existing complaints liable to be exacerbated should be transferred to other work, and those undertaking it provided with suitable supporting belts or corsets.

A. Meiklejohn

510. **Observations on Mercurialism in the Hat-makers of the Arno Valley.** (Rilievi e considerazioni sull'idrargirismo nei cappellifici del Valdarno)

L. CATTINELLI. *Rassegna di medicina industriale* [*Rass. Med. industr.*] **25**, 93–111, March–April, 1956. 36 refs.

511. **A Clinical and Statistical Study of Mercurialism in the Mercury Mining Industry of Monte Amiata.** (Studio clinico-statistico sul mercurialismo nell'industria mineraria del mercurio del Monte Amiata)

C. BARSI. *Rassegna di medicina industriale* [*Rass. Med. industr.*] **25**, 121–132, March–April, 1956. 1 fig., 22 refs.

[These two papers dealing with chronic mercury poisoning as it occurs in different environments should be read in the original by those interested, since it is difficult in an abstract to do justice to them.]

The Tuscan felt hat-making industry is located along the Arno valley to the south of Florence, and the first paper, from the Florence Institute of Industrial Medicine, gives a very full account of the various processes involved. Since fur, unlike wool, shows no tendency to "felt" spontaneously, the skins are treated with an acid nitrate solution of mercury and subjected to friction in the presence of heat and humidity until the softened hairs become closely interlaced. The felt is then shaped, cut, and prepared as required. These last processes are free from risk, but in the earlier stages an atmospheric concentration of mercury vapour as high as 4 μg. per cubic metre may occur, which is many times greater than the permissible limit. Symptoms of mercury poisoning among the exposed workers are generally more frequent and increase in gravity with length of service (and therefore with age). Both sexes are equally affected. Of 357 cases of mercury poisoning notified in this area between the years 1946 and 1953, there was some permanent disability in 161, reaching the compensation level (20% disability) in all but 13. Although changes in the process to reduce the amount of mercury used have been introduced with very good results in a few factories, they have not yet been generally adopted. Preventive measures recommended include the improvement of ventilation, the prohibition of eating in the factory except in a canteen, education, and careful supervision of the general health of the workers.

The second paper, which comes from the same source, gives a careful account of the processes involved in obtaining pure mercury from the cinnabar (HgS) mined at Monte Amiata, 30 km. south of Siena. The risk of mercurialism occurs during the processes of drying and roasting the ore and in the collection and "bottling" of the metal. Since the workers move about from one process to another, however, exposure is fairly general. From 1938 to 1954 107 cases of mercurialism in mine-workers in the area were notified, but only in 32 was the disability above 20%. General recommendations are made for prevention.

A comparison of the incidence of various symptoms and signs in cases of mercurialism among the miners with that among the hatters shows there to be some close similarities and some notable differences. Thus whereas the incidence of tremors (90 and 92·7%) and disorders of the mouth and gums (70 and 78%) is about equal in the two groups, gastro-intestinal disturbances occur in 63·5% of cases among the miners and in only 20% of those in the hatters, while erethism and headache occur in 77% and 51·8% respectively of the hatters compared with 14·9% and 6·5% of the miners. A blue line on the gums was present in 7·4% of affected miners and only 0·8% of affected hatters. In both papers the tremors are picked out for special description. They are usually fine, and detectable only with the arms outstretched and fingers separated; in addition (usually in the more serious cases) there are clonic contractions of the muscles, sometimes of a single limb but also at times general—the well-known "hatter's shakes" or the "jumps"—which are often worse at night. These tremors are regarded by both authors as the most distinctive signs of mercury poisoning.

W. K. Dunscombe

Forensic Medicine and Toxicology

512. **Treatment of Bromide Intoxication with Mercurial Diuretics**
A. E. HUSSAR and H. L. HOLLEY. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 100–106, Jan., 1956. 13 refs.

It is well known that the usual treatment of bromism by administration of sodium chloride leads to a very slow recovery, 3 to 6 weeks usually elapsing before symptoms of intoxication disappear. This is attributable to the fact that the bromide fraction of urinary halide is only about half the bromide fraction of serum halide, probably because the bromide ion moves across membranes more rapidly than the chloride ion and is thus more readily reabsorbed in the tubules. Since mercurial diuretics interfere with all reabsorption it may be expected that their administration will favour excretion of bromide.

In the treatment of 11 patients suffering from bromism at the Veterans Administration Hospital, Tuscaloosa, Alabama, meralluride (" mercuhydrin ") was given every 3 days and either sodium or ammonium chloride was given daily, the two salts sometimes being given in alternate 3-day periods. The treatment brought about a fall in the serum bromide concentration from an average of 236 mg. per 100 ml. to 75 mg. per 100 ml. in 9 days, symptoms of intoxication disappearing when the concentration fell to 100 mg. per 100 ml. Ammonium chloride was more effective than sodium chloride when given together with the mercurial, but not without it. It is suggested that patients suffering from bromism should be treated with 6 g. daily of ammonium chloride, with an intramuscular injection of 2 ml. of meralluride every 2 to 3 days. *V. J. Woolley*

513. **Kerosene Poisoning in Children**
W. D. MCNALLY. *Journal of Pediatrics* [*J. Pediat.*] **48**, 296–299, March, 1956. 6 refs.

During the period 1946–54 204 children suffering from kerosene (paraffin) poisoning were admitted to the City Hospital, Mobile, Alabama. Parental carelessness in leaving kerosene in glasses, cups, and beverage bottles accessible to the child was, it is stated, responsible for every case. The amount ingested varied from a few drops to 180 ml., and most of the patients were admitted to hospital within 45 minutes of taking the kerosene. The ages of the children ranged from 8 to 60 months, and 80·5% of them were negro. All had symptoms referable to the upper respiratory tract, but physical signs in the chest were slight in the majority of cases; nevertheless, 47% of the patients admitted during 1954 had radiological signs of pneumonia. Gastro-intestinal symptoms were relatively uncommon (27·5%). Listlessness and somnolence were prominent symptoms, even when the amount taken was small. Six deaths occurred, all within 23 hours of admission, the patients' ages ranging from 8 to 25 months.

Up to 1951 treatment was not standardized; some patients were given ipecacuanha, a few were given caffeine sodium benzoate, a few had gastric lavage, and nearly all were given antibiotics. The routine treatment now adopted consists in immediate gastric lavage with 2 oz. (57 ml.) of mineral oil, another ounce being left in the stomach. Penicillin is given on admission and its administration continued until the temperature is normal, and caffeine sodium benzoate, nikethamide, and oxygen are given when indicated. There have been no deaths in the last 3 years.

The author stresses the need for education of the general public as to the dangers of leaving kerosene in unidentified containers and within the reach of young children. He suggests that the use of empty beverage bottles for the storage of poisonous substances should be made illegal. [The compulsory introduction of colouring matter into kerosene sold for domestic purposes would seem likely to be a more effective measure, since in many of these cases the kerosene had evidently been transferred from its original container into a cup or other vessel in which it was indistinguishable in appearance from water. —EDITOR.] *Norval Taylor*

514. **Acute Barbiturate Poisoning**
P. M. G. BROUGHTON, G. HIGGINS, and J. R. P. O'BRIEN. *Lancet* [*Lancet*] **1**, 180–184, Jan. 28, 1956. 4 figs., 26 refs.

The results are recorded of analyses of specimens of blood, urine, and gastric contents from 36 patients (one of whom died) admitted to the Radcliffe Infirmary, Oxford, and from 10 persons found dead, after ingestion of commonly prescribed barbiturates. The majority of the 36 patients were unconscious on admission. The blood barbiturate level appeared to be related to the degree of consciousness; however, the long-acting barbiturates produced higher blood levels than similar doses of short-acting barbiturates. The mean blood levels on return to consciousness in 23 patients were 7 mg. (±2 mg.) per 100 ml. for the long-acting barbiturates, 3 mg. (±1 mg.) per 100 ml. for barbiturates with an intermediate action, and 1 to 2 mg. per 100 ml. for the short-acting drugs. Patients who had taken short-acting barbiturates usually recovered more rapidly than the others.

The administration of picrotoxin did not appear to influence the rate at which the blood level fell, but the findings suggested that when consciousness returned the blood level was higher in patients given picrotoxin than it was in untreated patients who had taken the same barbiturate. Analysis of gastric contents in 6 cases for which complete information was available showed that less than 4% of the ingested dose of the drug was recovered. If the specimen was obtained more than 12 hours after the drug had been taken the amount recovered

was insignificant. Single specimens of urine from a number of cases were examined, but no correlation was found between the urinary concentration and the degree of unconsciousness.

In only 2 of the 10 subjects who were found dead was the blood level significantly higher than in surviving patients who had taken the same drug. In general, only small amounts of barbiturate were found in the urine, liver, and kidney in these 10 cases, but the stomach and intestine usually contained large amounts, in contrast to the findings in the group of 6 surviving patients. The difference between the blood level produced by medicinal doses of barbiturates and that found in patients suffering from acute poisoning is discussed.

Norval Taylor

515. **Large Doses of Atropine. Low Toxicity and Effectiveness in Anticholinesterase Intoxication**
A. S. GORDON and C. W. FRYE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 1181–1184, Nov. 19, 1955.

Because of the potential use of anticholinesterase agents, such as organic phosphate compounds, as war gases and the increasing use of these compounds as insecticides the authors consider it important that their toxic hazards should be more widely known. At present, apart from other remedial measures such as removal from contamination, clearing of the airway, and artificial respiration, the best known medical antidote for organic phosphate poisoning is atropine, the tolerance of which is markedly increased in these cases. They therefore present a review of the results of treatment in 25 cases of organic phosphate poisoning reported in the literature in which sufficient data were given. "Parathion" was the poison except in a single case of tetraethylpyrophosphate poisoning. The initial dose of atropine varied between 0·48 and 2·1 mg., and the total dose received by the 16 survivors over a period of 24 hours varied between 0·65 and 24·0 mg.

The authors state that atropine should be given as soon as possible, the minimum initial dose being 2 mg., and thereafter further doses should be given at hourly intervals until signs of atropinization appear; patients with severe symptoms may require even larger doses. The usual signs of atropinization are drowsiness and restlessness, dryness of the mouth and mucous membranes, a dry, flushed skin, tachycardia, dilatation of the pupil, and urinary retention. In some cases disorientation, hallucinations, and even maniacal behaviour may occur, and these manifestations may be difficult to differentiate from those of the organic phosphate poisoning itself. The most reliable differentiating signs of over-atropinization were found to be the pupillary dilatation and dryness of the mouth and mucous membranes. It is of interest that in this small series only 3 of the survivors had received an initial dose of atropine as high as 2 mg. At the end of 5 hours' treatment, however, 7 of the 16 survivors had received 2 mg. or more, whereas of the 7 who died within 10 hours, only one had received this amount. The authors point out that apparently none of the cases was considered severe enough to require an initial dose of 2 mg. [It appears to be inferred that better results could have been obtained if larger doses of atropine had been given more promptly.]

R. Wien

516. **Medical Assessment of the Accident during the 24-hour Car Race at Le Mans.** (Le bilan médical de l'accident des Vingt-quatre Heures du Mans)
J. BARANGER. *Mémoires de l'Académie de chirurgie* [*Mém. Acad. Chir. (Paris)*] **82**, 238–242, Feb. 29, 1956. 1 fig.

On June 11, 1955, two cars competing in the 24-hour motor race at Le Mans came into collision opposite the stands while travelling at an estimated speed of 230 k.p.h. One of them plunged among the spectators, disintegrated, burst into flames, and was responsible for some 80 deaths and a similar number of serious injuries. The author, who was one of the surgeons responsible for treating the injured after this disaster, describes the measures taken and lists the various types of injury found. He attempts also to correlate the types of trauma inflicted in various zones of the affected area with the course of events after the car left the track [but owing to the almost complete lack of post-mortem data (necropsy having apparently been considered unnecessary by the legal authorities) and the wide discrepancies between the accounts of different eye-witnesses no useful conclusions are reached].

Gilbert Forbes

517. **A New Method of Identification of Human Blood.** (Sur une nouvelle méthode d'identification du sang humain)
J. RUFFIÉ and J. DUCOS. *Annales de médecine légale et de criminologie* [*Ann. Méd. lég.*] **36**, 17–21, Jan.–Feb., 1956. 4 refs.

The authors, working at the Medico-legal Institute, University of Toulouse, point out that the precipitin and complement-fixation tests for the identification of human blood in stains are both too delicate and too easily subject to errors in their performance. Recently, however, Vacher *et al.* (*Ann. Méd. lég.*, 1955, **35**, 29) described a new and simpler test based on a modification of the Coombs antiglobulin test. The present authors have devised independently a similar test, using Rh-positive erythrocytes coated with antibody from anti-D serum.

The test has been applied to bloodstains up to 4 years old which had been exposed to varying conditions of temperature and light on widely different materials such as canvas, wool, cotton, wood, and paper (including tarred paper), and at temperatures ranging from −30° C. to +37° C. The agglutination reaction was positive with all samples of human blood (and also those from some of the higher apes) but negative with blood from the sheep, dog, cat, and rabbit, and with that of birds such as the pigeon, fowl, and duck. Tests on material from an Egyptian mummy 4,000 years old [? blood] gave a negative result. The authors consider that the test is highly specific, is sensitive at dilutions up to 1 in 5,000, and that in view of its simplicity and objectivity it should be used in general medico-legal practice in preference to the classic methods hitherto employed.

W. K. Dunscombe

Anaesthetics

518. **Steroid Anesthesia in Man: Clinical and Cerebral Metabolic Effects**

G. S. GORDAN, N. GUADAGNI, J. PICCHI, and J. E. ADAMS. *Journal of the International College of Surgeons* [*J. int. Coll. Surg.*] **25**, 9–12, Jan., 1956. 1 fig., 15 refs.

In this article from the University of California School of Medicine, San Francisco, the effect of steroids on cerebral metabolism is discussed. Steroids with anaesthetic potency, such as deoxycortone, progesterone, and pregnandiol, have shown parallel inhibition of oxygen uptake by rat brain cells acting at the dehydrogenase level, and it has been demonstrated that the high oxygen uptake observed in castrated male rats can be reduced by the administration of various steroids. Experiments on rats, dogs, and monkeys having shown that 21-hydroxypregnanedione-3:20 (" viadril ") produced anaesthesia in these animals, the sodium salt of the hemisuccinate ester of this steroid was given intravenously to 8 human subjects without barbiturate or narcotic premedication; anaesthesia, consisting in loss of consciousness, analgesia, absence of corneal reflex, and muscular relaxation, occurred in 6 of the subjects after a latent period of 3 to 10 minutes. There was no respiratory depression and the profuse salivation which occurred in 2 cases was prevented by the previous administration of atropine sulphate. Pain over the course of the vein occurred if the infusion was given too rapidly or in a solution of greater concentration than 2·5 g. per 100 ml. No evidence of haemolysis was seen, as has been reported to be caused by certain other steroids.

The cerebral blood flow and cerebral metabolism were measured by the Kety–Schmidt technique before and 20 minutes after the infusion, and also in 12 patients anaesthetized with barbiturates; the results showed that cerebral blood flow and oxygen and glucose uptake in the two groups were almost identical.

The absence of respiratory depression and the action of the steroid at dehydrogenase level (as opposed to cytochrome level with the barbiturates) suggests that this compound is a true anaesthetic agent rather than a hypnotic. The authors suggest that the lag between administration and onset of anaesthesia may be due to the conversion of the compound to an active metabolite.

Raymond Vale

519. **Steroid Anesthesia in Man: A Clinical Report**

F. J. MURPHY, N. P. GUADAGNI, and F. L. DEBON. *Journal of the International College of Surgeons* [*J. int. Coll. Surg.*] **25**, 13–17, Jan., 1956. 4 refs.

In this paper is described the use of " viadril " (21-hydroxypregnanedione sodium succinate) as the basal anaesthetic in 125 surgical operations. The drug is a crystalline powder with a *p*H of 8·5 to 9·8 in solution in water; it causes no salt retention and no hormonal or demonstrable toxic effect.

After premedication with 50 to 75 mg. of pethidine hydrochloride, with or without hyoscine hydrobromide, a 2·5% solution of viadril was run into a 5% dextrose drip some distance from the vein to ensure adequate dilution, 1,500 mg. being given in about 5 minutes. This was followed by nitrous oxide and oxygen (3 : 1), or in some cases ether or cyclopropane. Muscle relaxants were used if required. If indicated, intubation was carried out about 10 minutes after administration and occasionally caused coughing but no severe laryngospasm. Gordan *et al.* (see Abstract 518) noted that the effect of viadril alone lasted only 18 to 73 minutes, depending on the dose, but when used in combination with other agents, as in this case, its effect was prolonged.

For abdominal operations additional relaxation with tubocurarine was required in a smaller proportion of cases than with thiopentone anaesthesia, and respiration could be controlled in some patients without the use of a relaxant. The operations performed included thoracic, neurosurgical, and general surgical procedures. The only complications were thrombophlebitis of the vein injected in 3 patients undergoing aortography, but this may have been due to the prone position and disease of the blood vessels.

The authors comment that viadril is a true anaesthetic with a potency between that of cyclopropane and ethylene, and does not produce the respiratory depression seen with thiopentone anaesthesia of comparable depth.

Raymond Vale

520. **Levallorphan (Lorfan) and Alphaprodine (Nisentil) in Anesthesia. Study of Effects in Supplementation of Nitrous Oxide–Oxygen–Thiopental (Pentothal) Sodium Anesthesia**

F. F. FOLDES, E. LIPSCHITZ, G. M. WEBER, M. SWERDLOW, and L. A. PIRK. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 168–175, Jan. 21, 1956. 1 fig., 15 refs.

The amount of thiopentone required for general anaesthesia can be reduced by intravenous administration of analgesics. Alphaprodine is closely related to pethidine, but is 2½ to 3 times more powerful than the latter and its duration of action is considerably shorter. It has the disadvantage that it causes marked respiratory depression, but it has been found that levallorphan protects against this depression (of respiratory depth rather than of respiratory rate) without counteracting the hypnotic or analgesic effects of alphaprodine.

Alphaprodine and levallorphan were given in addition to nitrous oxide, oxygen, and small amounts of thiopentone to 852 patients, and the results compared with those obtained in 756 patients in whom anaesthesia was supplemented with alphaprodine only. The two supplementary drugs were given separately by injection and relaxants were administered when necessary. The thiopentone requirements were considerably less in the

patients receiving both alphaprodine and levallorphan than in those receiving alphaprodine alone. Satisfactory operative conditions were produced without the use of thiopentone in 27% of patients subjected to extraperitoneal operations. In both groups of patients the requirements of thiopentone and alphaprodine in mg. per minute were inversely proportional to the duration of anaesthesia. The proportion of patients who reacted to stimulation at the end of the operation was somewhat higher in the alphaprodine–levallorphan group than in the controls. Moreover, the state of consciousness in the former group was far superior to that of the controls. No major post-anaesthetic complications were encountered. *W. Stanley Sykes*

521. **Controlled Analgesia with Continuous Drip Meperidine. Analysis of One Thousand Cases**
H. M. AUSHERMAN, W. K. NOWILL, and C. R. STEPHEN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 175–179, Jan. 21, 1956. 5 figs., 17 refs.

In a trial investigation at Duke Hospital, Durham, North Carolina, meperidine was given by continuous drip infusion to 800 patients during thiopentone–nitrous-oxide–oxygen anaesthesia for plastic, orthopaedic, and other extra-abdominal procedures not requiring deep anaesthesia. In 200 cases, used as a control, the meperidine was omitted. The drug was given in a 5% dextrose solution containing 0·5 mg. per ml., rapidly until the respiration began to slow down, then as required. Relaxants were used when indicated. Respirations were not allowed to fall below 10 per minute, and were assisted if necessary. Tidal volume was not as a rule reduced, but minute volume was, and this was considered to be due to the fall in respiratory rate. Carbon dioxide retention did not seem to occur, as shown by determinations in 30 cases. By the use of meperidine the requirement of thiopentone was reduced by 48% in the whole series, but by only 29·4% in cases in which the operating time exceeded 4 hours.

In the authors' view meperidine is a valuable addition to the list of non-explosive drugs that can be used in anaesthesia. They consider that there is less risk of overdosage when it is given in dilute solution as a continuous infusion than when given by intermittent injection. *W. Stanley Sykes*

522. **Continuous "Nisentil" and Suxamethonium in Anaesthesia**
F. M. LANCASTER and J. LEVIN. *British Medical Journal* [*Brit. med. J.*] **1**, 381–383, Feb. 18, 1956. 1 fig., 13 refs.

The infusion of suxamethonium as a continuous intravenous drip has proved a beneficial method of obtaining relaxation during anaesthesia, but on its discontinuance there may be undesirable reflex overactivity and a too rapid return to consciousness. To obviate these drawbacks some anaesthetists have used pethidine. The present authors, working at St. George's and Hackney Hospitals, London, have used "nisentil" (alphaprodine), a substance which is pharmacologically very similar to pethidine but whose action is said to be shorter and more rapid, in the performance of 120 abdominal operations as a supplement to nitrous-oxide–oxygen anaesthesia, muscular relaxation being obtained by continuous infusion of a suxamethonium–nisentil solution containing 5 mg. of nisentil and 50 mg. of suxamethonium in each 50 ml. of solution.

Troublesome reflex disturbances were notably absent; nearly half the patients (47%) could be roused while still in the operating theatre, while the remainder recovered consciousness in about half an hour after operation; also the residual analgesic effect of nisentil diminished postoperative restlessness and discomfort. Used in this way, nisentil proved a satisfactory drug and is considered superior to pethidine. *Ronald Woolmer*

523. **Electrocardiographic Changes during Hypothermia and Circulatory Occlusion**
C. E. HICKS, M. C. MCCORD, and S. G. BLOUNT. *Circulation* [*Circulation* (*N.Y.*)] **13**, 21–28, Jan., 1956. 7 figs., 14 refs.

The authors present, from the University of Colorado School of Medicine, Denver, an analysis of the electrocardiographic changes observed in 25 patients, ranging in age from 3 months to 36 years, undergoing cardiovascular surgery under hypothermia. Progressive slowing of the heart rate occurred with decreasing temperature and was accentuated by circulatory occlusion. Thus the average heart rate for the group was 122 beats per minute before cooling, 55 per minute just before circulatory occlusion, and 32 per minute during occlusion. With decreasing temperature the P–R interval increased and the QRS and Q–T intervals widened. The only constant changes in the configuration of QRS were the appearance of a Q wave and the development of an R′ or a notched R wave. The amplitude and direction of the T wave changed frequently, but with no constant pattern. The S–T segments showed frequent displacement, but this could not be correlated with any factor.

In 18 instances the first alteration in rhythm was the appearance of an ectopic atrial focus of impulse formation with a 1 : 1 atrio-ventricular response. The site of the pacemaker appeared to vary from the sinus node to an ectopic atrial focus or to a nodal focus. The temperature at which a sinus rhythm was replaced by a wandering pacemaker was related to age; thus, the younger patients maintained a sinus mechanism during a greater reduction of temperature than older patients. The wandering pacemaker was replaced by a rapid ectopic atrial focus, consisting of atrial fibrillation in 12 patients and atrial flutter in 3, and again there was a correlation between age, temperature, and the occurrence of atrial fibrillation. Occlusion of the circulation was associated with marked alteration in the existing rhythm, resulting in an idioventricular rhythm in 10 cases, cardiac standstill for 10 seconds or longer in 13, and ventricular fibrillation in 3. These ventricular rhythms were immediately replaced by a supraventricular rhythm on re-establishment of the circulation in all but 2 of the patients, both of whom died as a direct result of the arrhythmia. Myocardial hypoxia and trauma incident to cardiac manipulation are considered to be the major factors responsible for the occurrence of these ventricular arrhythmias. *William A. R. Thomson*

Radiology

524. **A Report on the Use of Convergent Beam X-ray Therapy**
G. E. FLATMAN and R. E. ELLIS. *British Journal of Radiology* [*Brit. J. Radiol.*] **29**, 139–147, March, 1956. 16 figs., 11 refs.

The Siemens Convergent Beam *X*-ray Therapy Unit installed at the Middlesex Hospital, London, is described, and its use from November, 1952, to February, 1955, in the treatment of 192 patients discussed. Two methods of operation have been used: (1) convergent beam therapy, in which the beam travels from the centre to periphery, and (2) peripheral convergent beam therapy in which only the periphery is used. The authors found with experience that the latter method was the more useful. The machine was used at 200 kV and 20 mA, with a H.V.L. of 1 mm. Cu. The dosage calculations were based on the dose measured in air at the convergent point. Several isodose curves are reproduced.

The clinical applications are described, but the number of cases treated was considered too small for statistical analysis. The authors found the unit most useful for the treatment of pituitary tumours by two opposing ports, 8 patients having been treated by this method. Tumours of the nasopharynx were among the conditions treated most successfully, and tonsillar tumours were also frequently treated. Hilar masses in the thorax were considered to present too large a volume of tissue of an unsuitable shape for this method of therapy, and in the pelvis, although the unit was used successfully for the palliative treatment of pelvic masses, its use is not recommended for parametrial irradiation after the insertion of radium.

In general, it was considered that treatment with this unit caused less constitutional disturbance and skin reaction than treatment with conventional apparatus.

E. D. Jones

525. **Rotation Therapy with a 2 MeV Van de Graaff Generator**
K. F. ORTON. *British Journal of Radiology* [*Brit. J. Radiol.*] **29**, 186–192, April, 1956. 10 figs., 9 refs.

526. **A Report on 35 Cases of Malignant Tumours of Nasopharynx**
D. STEVENS. *Journal of Laryngology and Otology* [*J. Laryng.*] **70**, 147–157, March, 1956. 19 refs.

The author reports the results of treatment in 35 cases of malignant disease of the nasopharynx admitted to Cardiff Royal Infirmary between 1948 and 1954. [Owing to the small number of cases and the brief follow-up period the results here recorded can give little idea of the value of the treatment employed.] An interesting description is given of the anatomical relations of the nasopharynx and the consequent symptomatology of tumours in this region. The differential diagnosis of primary and secondary disease is discussed, and a new diagnostic sign—" cavernous nasal breathing "—is described. The treatment of these cases was mainly by irradiation of the primary lesion and irradiation or excision of lymph nodes according to the histology.

[The author's statement that squamous carcinomata are relatively resistant to radiation will not find general agreement, and the suggested method of irradiation of the nasopharynx—as a primary form of treatment—by means of a radium applicator through a palatal window would seem less promising than use of x rays at the higher voltages, which makes easier the adequate irradiation of a cavity surrounded by bone.]

V. M. Dalley

RADIODIAGNOSIS

527. **The Radiological Diagnosis of Cancer, Apparently Primary, of the Pleura.** (Le diagnostic radiologique des cancers apparemment primitifs de la plèvre)
P. DUTILH. *Journal de radiologie, d'électrologie et Archives d'électricité médicale* [*J. Radiol. Électrol.*] **36**, 833–844, Nov.–Dec., 1955. 16 figs., 12 refs.

The author discusses the radiological diagnosis, in 2 cases seen at the Hôpital de Val-de-Grâce, Paris, of diffuse primary carcinoma of the pleura, a rare condition representing only 0·03 to 0·07% of all cancers. The diagnosis is made difficult not only on account of the rarity of the condition, but also because of its similarity, clinically and radiologically, to primary carcinoma of the bronchus invading the pleura. Some authors, in emphasizing the difficulties of pathological diagnosis, have denied the existence of the lesion, but more recent workers have distinguished the characteristics of these tumours.

They occur most frequently in men between the ages of 40 and 50, the onset is slow, and patients do not usually come for treatment until the condition is far advanced. Occasionally, especially in young patients, the onset may be rapid. The effusion is serofibrinous or haemorrhagic with lymphopenia, but there is nothing characteristic in its appearance. Owing to the insidious onset the whole of the hemithorax is frequently found to be occupied by a uniform opacity at the first radiological examination. If seen early, a diffuse, peripheral, flat tumour may be visualized, most often on the anterior wall. If fluid is present it will collect again rapidly after aspiration, so that radiographs must be taken within a few hours. Erosion of the ribs is rare, except in the late stages. Tomography may help in showing the underlying condition, and examination after aspiration and re-insufflation of the pleural space with air may be diagnostic. Pulmonary signs with pleural effusion are never found in an early primary pleural tumour. A polycystic appearance of the pleural surface is charac-

teristic, but bronchography will not reveal any abnormality. Metastasis from a primary pleural tumour is stated to be very rare. *John H. L. Conway-Hughes*

528. **Percutaneous Selective Angiography of the Main Branches of the Aorta. (Preliminary Report.)** [In English]
P. ÖDMAN. *Acta radiologica* [*Acta radiol. (Stockh.)*] **45**, 1–14, Jan., 1956. 12 figs., 12 refs.

In the usual method of visualizing the branches of the aorta by aortography or by angiocardiography the possibilities of directing the contrast solution so that the major part enters one particular vessel are small, while the risk of the medium entering sensitive vascular areas, particularly the brain and kidneys, in toxic concentration may be considerable. Furthermore, the presence of medium in irrelevant branches may obscure pathological changes. For these reasons a selective angiographic method allowing of visualization of each branch of the aorta separately is highly desirable. Previously described methods have involved exposure of the brachial, carotid, or femoral artery and the passage of a catheter under fluoroscopic control. Technical difficulties and the risks related to surgical errors, postoperative thrombosis, or wound infection, have limited the applicability of these methods.

In this paper from Södersjukhuset, Stockholm, the author describes a percutaneous technique, for which he uses a radio-opaque polythene catheter. This may be softened by immersion in hot water (above 72° C.) and is then cooled quickly while it is being shaped to the desired curve. The distal bore of the catheter is narrower than the rest of the lumen, and close to the tip there are lateral holes directed away from the tip which help to reduce considerably the displacement of the catheter during injection. The catheter is inserted percutaneously through the femoral artery by Seldinger's technique, its direction being controlled by fluoroscopy. So far, 20 examinations have been carried out. Each arterial branch requires a specially shaped catheter, and detailed descriptions of some of these are given. No difficulties have been encountered in carrying out the procedure and no complications have occurred.

John H. L. Conway-Hughes

529. **Percutaneous Catheterization of the Renal Artery.** [In English]
P. EDHOLM and S. I. SELDINGER. *Acta radiologica* [*Acta radiol. (Stockh.)*] **45**, 15–20, Jan., 1956. 7 figs., 5 refs.

Reports of damage to the kidney during aortography have been not infrequent. However, by direct injection into the renal artery the amount of contrast medium can be controlled and the opposite kidney need not be exposed to the contrast medium, as is the case in aortography. Working at the Karolinska Hospital, Stockholm, the authors use a polythene cathether which is introduced percutaneously by Seldinger's technique, the shape of the catheter being such that the perpendicular distance from the tip to the straight part is somewhat greater than the diameter of the aorta. It has been found best to catheterize the femoral artery on the same side as the kidney to be examined. An image intensifier, although not essential, has proved of great help.

The authors state that there is no unpleasant sensation when the opaque medium is injected into the renal artery, whereas a feeling of burning in the pelvis or legs is produced when even small amounts are injected into the aorta. The technique, described in detail, has failed in one case in which a sinuous aorta and iliac artery impeded free movement of the catheter, but was successful in 8 other cases. The dose of contrast medium varied from 4 ml. of 35% plus 1 ml. of 70% " umbradil " up to 10 ml. and 7 ml. respectively of this substance. The occurrence of aberrant arteries directly originating from the aorta (the frequency of which is stated to be 22·9% of cases) diminishes the value of selective angiography. It should be borne in mind also that there is a risk that a pathological process may be situated in an area supplied by an artery which is not visualized; such an area may also be misinterpreted as an avascular tumour.

John H. L. Conway-Hughes

530. **Selective Angiography of the Abdominal Aorta with a Guided Catheter.** [In English]
H. TILLANDER. *Acta radiologica* [*Acta radiol. (Stockh.)*] **45**, 21–26, Jan., 1956. 6 figs., 8 refs.

The author describes, from Centrallasarettet, Västeras, Sweden, an original technique of selective angiography of the abdominal aorta for which he has devised a catheter with a flexible jointed point which can be guided by means of a magnetic field. An electromagnet is placed under the examination table (which must be of non-magnetic material) so that it can be moved both along the long axis of the table and at right angles to it. The *x*-ray tube is placed in a horizontal position at one side of the table and the fluorescent screen at the other. The catheter itself is a cardiac catheter 120 cm. long made of plasticized cloth, and the flexible point, made of gold-plated soft iron approximately 35 mm. in length, consists of four cylindrical sections linked by ball-and-socket joints, each of which permits a range of movement of 20 degrees in all directions. The catheter is fitted with a two-way stopcock, through which heparinized saline solution can be introduced on one side and the contrast medium on the other. The latter is injected under pressure in approximately 10 seconds, thus overcoming the frictional resistance in the long catheter and the tip.

In performing angiography the catheter is introduced into the exposed radial artery about 10 cm. distal to the flexure of the elbow and guided towards the descending aorta under fluoroscopic control, the patient being supine. For examination of the renal arteries it is best to turn the patient on to the same side as the kidney to be examined. About 10 ml. of medium is needed for a renal angiogram and 15 ml. for a coeliac angiogram; the concentration should not exceed 35%. Some premedication is necessary. About 30 angiographic examinations have been carried out so far; in a few of the earlier cases spasm occurred in the brachial artery which prevented the examination being completed. The author

agrees that the main drawbacks of the method are the rather complicated equipment required and the additional risk of the surgical procedure.

John H. L. Conway-Hughes

531. **Extraintestinal Roentgen Manifestations of Intestinal Lipodystrophy**

W. R. EYLER and H. P. DOUB. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 534–536, Feb. 18, 1956. 5 figs., 9 refs.

In this short paper from the Henry Ford Hospital, Detroit, 4 cases of intestinal lipodystrophy are described. The principal clinical features were recurrent diarrhoea and polyarthritis, with pigmentation of the skin and enlargement of the mediastinal, retroperitoneal, and peripheral lymph nodes. Radiologically, all the cases showed a deficiency pattern in the small bowel, the mucosal outline being coarse and the barium column showing flocculation, clumping, and discontinuity; other radiological findings were enlarged lymph nodes in the thorax and changes in the sacro-iliac joints suggestive of a Marie–Strümpell type of arthritis. None of the radiological findings, however, is specific, and diagnostic confirmation depends on lymph-node biopsy.

Sydney J. Hinds

532. **Water-soluble, Nonabsorbable Radiopaque Mediums in Gastrointestinal Examination**

L. A. DAVIS, KEE-CHANG HUANG, and E. L. PIRKEY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 373–375, Feb. 4, 1956. 4 figs., 3 refs.

Barium sulphate, the standard opaque medium in general use for the radiological examination of the gastrointestinal tract, has in general given good results, but it forms an insoluble, particulate suspension in water, and chiefly because of this gives poor delineation of the mucosal pattern. At the University of Louisville, Kentucky, the authors have therefore been trying two non-viscous organic iodine compounds designed for urography, namely, sodium acetrizoate (" urokon sodium ") and sodium diatrizoate (" hypaque "). These are true solutions, contain no particulate matter, and laboratory experiments have shown that they are only slightly absorbed from the intestine and have no toxic effects other than a mild purgative action on occasion. However, they are unpleasant to taste, and so far have been used mainly in cases where a gastric tube was *in situ*.

Using these media they have been able to detect small ulcers which examination with the conventional barium meal did not disclose. The media can also be passed through a Miller–Abbott tube to show small segments of the small intestine. The authors have used them in concentrations of up to 70% for adults and of 50% or less for children. The media are of lower viscosity than barium and are non-toxic if accidentally introduced into the tissues or body cavities. Also, there is considerable advantage in their use in cases in which barium would be likely to inspissate and predispose to obstruction, such as in the investigation of megacolon. Their main disadvantages are: high price, small fluid volume which is inadequate for filling the stomach (except in the infant), and bitter taste.

A. M. Rackow

533. **The Use of Pro-banthine and of Baridol in the Visualization of the Mucosal Pattern of the Small Intestine**

J. GLAZEBROOK, C. MONGEON, and E. WONG. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] 74, 280–285, Feb. 15, 1956. 8 figs., 11 refs.

In an attempt to compare the value in the radiological examination of the small intestine of " baridol ", a colloidal suspension of barium sulphate stabilized by micro-pulverization, with that of an " ordinary " barium sulphate suspension, and at the same time to assess the effect of " pro-banthine " (propantheline) on the visualization of the mucosal pattern, 26 barium-meal examinations were carried out on 11 healthy subjects, using varying concentrations of the media and varying doses of propantheline, at the St. Boniface Hospital (University of Manitoba). The authors found that the colloidal preparation gave better visualization of the small intestinal pattern, and that even better detail was obtained with propantheline.

[The use of colloidal suspensions of barium is almost essential in small-intestinal studies, and anticholinergic drugs probably help. But so many variable factors are involved that it is difficult to prove the superiority of any particular routine or preparation, and conclusions drawn from a trial carried out on a small number of healthy subjects are unconvincing and not necessarily valid for the examination of patients with severe functional disorder and structural disease.] *Denys Jennings*

534. **Autoradiography in the Study of Bone Fractures.** (Радиоавтография при изучении переломов костей)

V. A. POLYAKOV. *Вестник Рентгенологии и Радиологии* [*Vestn. Rentgenol. Radiol.*] **31**, 69–73, No. 1, Jan.–Feb., 1956. 9 figs., 26 refs.

The author describes a method for the study of the processes of healing in fractured bones by autoradiography after the administration of radioactive isotopes to animals which have been subjected to experimental bone fractures, the isotopes used being ^{32}P, ^{89}Sr, and ^{45}Ca. At various intervals after the fracture thin slices of the fractured bone were placed in contact with photographic plates, the resulting image showing where the concentration of radioactivity was highest.

It was demonstrated that the concentration of mineral salts at the site of a fracture had already begun within a few days of the injury, before there was any radiographic evidence of callus. Moreover, the mineral metabolism of the animal was affected not only at the site of the fracture, but also in remote parts of the body, these general changes continuing for a considerable time. Concentration of the isotopes at the site of the injury continued for 12 to 18 months after consolidation of the fracture had begun. Plating or pinning of the fracture always produced changes in the general mineral metabolism of the skeleton in addition to local changes. It was concluded that accumulation of the radioactive isotopes in the fractured bones was accomplished not by diffusion through the tissues, but through the blood stream, and took place only in the living bone. Considerable changes in mineral metabolism were observed in cases of traumatic osteomyelitis.

A. Orley

History of Medicine

535. **The History of Osteopsathyrosis (Osteogenesis Imperfecta).** (Die Geschichte der Osteopsathyrosis (Osteogenesis imperfecta))
B. VALENTIN. *Centaurus* [*Centaurus* (*Kbh.*)] **4**, 132–147 1955 [received March, 1956]. 7 figs., bibliography.

Osteopsathyrosis (osteogenesis imperfecta) is widespread throughout the world and has been recognized for over 200 years, though of the numerous articles on the disease in the medical literature, few contain anything but case reports. Looser pointed out in 1906 that the intrauterine and postnatal forms of the disease were identical in origin, and this is generally agreed. More recently Cocchi has gone a step further and claimed that three types of the disease can be identified—foetal osteogenesis imperfecta (Vrolik), osteopsathyrosis (Lobstein) (with 2 subtypes), and the triad of hereditary fragilitas osseum (blue skin, deafness, and fragility). The disease is due to a disturbance of bone development, and in particular of new bone formation. There is no failure of calcification, but a disturbance of the bone-forming elements, possibly with increased bone absorption. As a result there is reduced resistance to bending stresses, which results in fractures from trivial causes.

The first report of a case, published in 1674 by Nicholas Malebranche, was that of an idiot child who had multiple fractures of the limbs " such as a criminal suffers after being broken on the wheel ", and the condition was attributed to the mother having witnessed such an event during her pregnancy. The same view was taken of many subsequent cases, even those reported by Buffon (1707–88). The first published illustration of a case is of an 8-month foetus described by Bordernave (1728–82) before the Academy of Science in Paris in 1763. The first suggestion that the condition was of constitutional origin was made in 1788 by Ekmann in a thesis published in Uppsala. With the spread of scientific knowledge, the descriptions of cases published after this date were much more complete and accurate, and began to include details of the post-mortem examination. A familial tendency was first detected by Strack in 1806, who described the delayed onset of the disease in three brothers, one of whom, Edmund Axmann, subsequently became a doctor. In 1831 Axmann described changes in the sclera which he had observed in himself and his brothers, and first pointed out that this was characteristic of the syndrome, although his observation went unnoticed by subsequent authors.

In the second volume of his *Traité d'Anatomie Pathologique*, published in 1833, Lobstein first clearly distinguished the disease under the name of " osteopsathyrosis idiopathica " and used the expression *casser comme du verre* to emphasize the exceptional fragility of the bones. Even so, other authors continued to attribute the condition to foetal rickets and later to infantile osteomalacia. More accurate observations were made by Vrolik (1801–63) who finally differentiated the disease from rickets and gave it the name of " osteogenesis imperfecta ", which has since been more generally used than the earlier name of osteopsathyrosis. Fragility of the bones was the only feature generally recognized until blueness of the sclerotics was reported afresh as a new observation in 1896, in 1900, and again in 1913. The third characteristic feature, deafness, was first mentioned by Dighton in 1912. Ekmann had already emphasized the striking enlargement of the skull in 1788, while a further sign, the general laxity of the joints which has often led to recurrent dislocation, was mentioned by Axmann.

Among the well-known persons who have suffered from the disease may be mentioned Honoré de Balzac, whose blue sclerotics were described by Gautier, and Toulouse-Lautrec the painter. *J. G. Bonnin*

536. **Epidemics of Jaundice in the 1850s.** (Les épidémies de jaunisses vues par les praticiens de 1850)
E. CHABROL. *Bulletin de l'Académie de médecine* [*Bull. Acad. Méd.* (*Paris*)] **140**, 114–118, Feb. 28, 1956. 6 refs.

The author discusses two epidemics of jaundice occurring in the early 19th century, the first of which, originally reported by Chardon in 1842 to the French Royal Academy of Medicine, occurred at Chasselay on the northern slopes of the Mont d'Or near Trevoux. The main symptoms were malaise, anorexia, epigastric discomfort, pain in the right hypochondrium, jaundice, and bile in the urine. The youngest patient was 4 years old, but most of the others were adults. The epidemic lasted 3 months and there were no deaths. Chardon's suggestion that the outbreak was due to a distinct disease entity —" essential epidemic jaundice "—was, however, rejected by the Epidemic Commission of the Academy, which concluded that the jaundice was a secondary or symptomatic condition.

The second outbreak occurred in the prison of Gaillon in 1859 and was originally reported by Carville in 1864. The 1,665 prisoners included 540 children, 15 of whom became jaundiced, though none died, whereas of the 1,125 adults, 32 sickened and 11 died, 7 being between 40 and 50 years old. Carville's report was much more detailed than that of Chardon and he was able to establish the distinctive nature of the disease.

After a lengthy and verbose discussion of the differential diagnosis, the author concludes that both epidemics were due to what is now called infective or viral hepatitis rather than to leptospirosis or typhoid fever. In the year of the Gaillon outbreak Monneret published his monograph on " essential haemorrhagic jaundice ", the description of which leaves no doubt that it was what we now term leptospirosis, an account of which had been published 10 years previously by the Dublin physician Graves. The English physician Budd, in his *Diseases of the Liver* published in 1845, recorded a

number of observations of epidemic jaundice, but made no distinction between the two types. To Carville must therefore go the credit of the first description of infective hepatitis as an epidemic disease distinct from leptospirosis. *I. M. Librach*

537. **Joan d'Alós and the Doctrine of the Circulation of the Blood**

J. PI-SUNYER. *Yale Journal of Biology and Medicine* [*Yale J. Biol. Med.*] **28**, 415–418, Dec.–Feb., 1955/6. 1 fig., 3 refs.

The opposition to the new doctrine of the circulation of the blood expounded by Harvey in his *Exercitatio Anatomica de Motu Cordis*, published in 1628, was only gradually overcome during the 17th century. It was led by the ultraconservative Sorbonne school in Paris and shared by most of the Spanish medical schools. However, a notable exception was the medical school of Barcelona, which provided two defenders of the circulation theory in Franceso Morelló and Joan d'Alós. It is with the last named that the present author is concerned.

Joan d'Alós i Serradora was born in 1617, the son of the Protophysician of the Princedom of Catalonia. His life was actively spent in political and medical circles in Barcelona, of which city he became an alderman in 1666, a captain in the medical corps of the army in 1684, and a representative in 1690. As Professor of Medicine at the University of Barcelona, to which post he was appointed in 1664, he taught anatomy, " aphorisms ", and pharmacy. He died in 1695.

Three books by d'Alós are extant. The first, entitled *Pharmacomedica Dissertatio de Vipereis Trochiscis*, was published in Barcelona in 1664, and is a study of pharmacognosy and therapeutics. The second, *Pharmacopea Catalana sive Antidotarium Restitutium et Reformatum* (Barcelona, 1666), consisted of a monograph on the local pharmacopoeia. But d'Alós's most important work is his *De Corde Hominis Disquisitio Physiologico-Anatomico*, a beautiful volume of 247 pages which appeared in 1694. In this Alós describes Harvey's doctrine in detail, stressing its great importance and the necessity for its general acceptance. He does not appear, however, to have confirmed Harvey's theory experimentally, except possibly in minor details. The book contains a very interesting section on blood transfusion in which d'Alós discusses its possible use in rejuvenation and therapeutics, and the feasibility of employing human blood. Further chapters are enriched with original observations on the heart, arteries, and pulse. The manner in which d'Alós refutes the arguments of the opponents of the theory shows that he distrusted the traditional methods of disputation and formal reasoning. In his insistence on the necessity of precise observation he was far ahead of his time. Despite the neglect of d'Alós by Spanish medical historians, he was clearly an important figure in the history of the doctrine of the circulation.

[The author gives locations in Barcelona libraries for each of d'Alós's books. In London, the library of the British Museum contains copies of the *De Corde Hominis*, 1694, and the *Pharmacomedica Dissertatio* of 1664. The Wellcome Historical Medical Library possesses a copy of the *Pharmacopea Catalana*, for which the present author gives the date as 1666, but this would seem to need verification since the copy in the Wellcome Library is dated 1686, which is also the date given in bibliographical sources.] *F. M. Sutherland*

538. **Mozart and the Doctors, his Illnesses, and his Death.** (Mozart und die Ärzte, seine Krankheiten und sein Tod)

A. GREITHER. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **81**, 121–124 and 165–169, Jan. 27, and Feb. 3, 1956. 23 refs.

It has been generally assumed that the cause of Mozart's death in 1791, a few weeks before his 36th birthday, was tuberculosis. The theory that his early death was due to poisoning—rumours to this effect began to circulate immediately after his death—has only very few supporters nowadays; among those suspected was the composer Salieri (who is alleged to have confessed to this deed before his death in 1826) and the Freemasons who, it was said, wanted to take revenge because Mozart had revealed their secret rites in his opera " The Magic Flute ".

A third theory (first put forward by Barraud in 1905) which attributes the composer's death to chronic nephritis has received but little attention. The author of the present paper supports this theory, basing his conclusions on a scrutiny of the many accounts of Mozart's death and on an analysis of a number of letters in which the composer himself mentions details of the illnesses which befell him in the last years of his life. These are stated to show that Mozart suffered a first attack of pyelonephritis in 1784 at the age of 28, had several relapses in the following years, and finally died in uraemic coma. The author attributes to the chronic nephritis the depression which clouded Mozart's last weeks and which found its tragic climax in his delusions about the mysterious circumstances under which he received the commission to write a Requiem. An attempt is also made to explain the nature of some of the many illnesses from which Mozart suffered from his early childhood onwards. The letters of Leopold Mozart, the composer's father, refer frequently to these illnesses (described as " catarrhs " and " raging fevers "), which several times had forced him to interrupt the tours on which he had taken the young Wolfgang and his sister. The father is severely blamed because in his ambition he never allowed the children sufficient time to recover completely from these disorders, this fact being regarded as the principal cause of the seriously weakened condition in which the composer spent most of his short life. In addition to many minor illnesses Mozart suffered in his childhood several major illnesses, including rheumatic fever in 1763, at the age of seven, typhoid fever (together with his sister) in 1765 while on a tour in the Netherlands, a relapse of the rheumatic fever the following year, and smallpox in 1768. The author also gives short biographical sketches of some of the doctors, Austrian, German, and Dutch, under whose care Mozart came as a patient. *A. Fessler*